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=> fil wpix
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=> d all abeq tech abex tot

L47  ANSWER 1 OF 10  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2004-313738 [29]    WPIX
CR   2003-801085 [75]
DNN  N2004-249776        DNC C2004-119121
TI   Treating cancer and metabolic diseases by administering a multi-specific
     antibody having a targeting arm that binds to an antigen and a capture arm
     that binds to a polymer conjugate comprising a therapeutic agent.
DC   A96 B04 C06 D16 K08 S03
IN   GOLDENBERG, D M; GRIFFITHS, G L; HANSEN, H J
PA   (IMMU-N) IMMUNOMEDICS INC
CYC  1
PI   US 2004043030   A1 20040304 (200429)*      24    G01N033-574
ADT  US 2004043030 A1 Provisional US 2001-308605P 20010731, CIP of US
     2002-209592 20020731, US 2003-456580 20030609
PRAI US 2001-308605P      20010731; US 2002-209592       20020731;
     US 2003-456580       20030609
IC   ICM  G01N033-574
     ICS  A61K039-395
AB   US2004043030 A UPAB: 20040505
     NOVELTY - Diagnosing or treating a disease or disorder, involves
     administering to a tissue a multi-specific antibody (I) or antibody
     fragment, comprising a targeting arm that binds to an antigen on the
     target site, and a capture arm that binds to a polymer conjugate, and
     administering to the tissue a polymer conjugate that binds to the capture
     arm, the polymer conjugate comprising a polymer conjugated to a diagnostic
     or therapeutic agent.
          DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for
     photodynamic diagnosis or treatment of a disease or disorder or
     intravascular or endoscopic method for diagnosing or treating a disease or
     disorder, involves administering to a tissue a multi-specific antibody or
     antibody fragment, comprising a targeting arm that binds to an antigen on
     the target site, and a capture arm that binds to a polymer conjugate, and
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administering to the tissue a polymer conjugate that binds to the capture arm, the polymer conjugate comprising a polymer conjugated to a diagnostic or therapeutic agent.

ACTIVITY - Cytostatic; Antiinflammatory; Nootropic; Neuroprotective; Antiatherosclerotic; Vasotropic; Thrombolytic; Immunosuppressive; Nephrotropic; Dermatological; Antirheumatic; Antiarthritic; Hemostatic; Analgesic; Antidiabetic; Antiulcer; Hepatotropic; Thyromimetic; Antiallergic; Antibacterial; Fungicide; Virucide; Antiparasitic; Protozoacide; Antianemic.

A subject who has colon cancer that expressed the CEA antigen was given a 100 mg/m2 dose of the bi-specific antibody hMN-14 multiply 374 F(ab')2 multiply Fab'. After 24 hours, the subject was then given an equimolar dose of the indium coupled of the AcLys (diethylenetriaminepentaacetic acid)Glu6(SN-38)6Lys(diethylenetriaminepent aacetic acid)NH2 diethylenetriaminepentaacetic acid-polymer-drug, conjugate. The diethylenetriaminepentaacetic acid-polymer-drug was localized selectively at the tumor due to the pretargeting with the multi-specific antibody, causing a high concentration of the active agent SN-38 to also be localized. Over time, free SN-38 was released from the localized conjugate, exerting a therapeutic effect on the tumors.

MECHANISM OF ACTION - Immunotherapy.

USE - The method is useful for diagnosing or treating a disease or disorder chosen from cancer (esophageal, gastric, colonic, rectal, pancreatic, lung, breast, ovarian, urinary bladder, endometrial, cervical, testicular, renal, adrenal and liver cancer, solid tumor, B-cell malignancy or T-cell malignancy); cardiovascular lesion; an inflammatory disease; neurodegenerative disease; metabolic disease; and an infectious disease. The B-cell malignancy is chosen from indolent forms of B-cell lymphomas, aggressive forms of B-cell lymphomas, chronic lymphatic leukemias, acute lymphatic leukemias, and multiple myeloma. The solid tumor is chosen melanoma, carcinoma (preferably renal carcinoma, lung carcinoma, intestinal carcinoma, and stomach carcinoma), glioma and sarcoma. The cardiovascular lesion is chosen from infarct, clot, embolus, atherosclerotic plaque and ischemia. The neurodegenerative disease is Alzheimer's disease. The metabolic disease is amyloidosis, where the antibody binds amyloid. The disease or disorder is displaced or ectopic normal tissue chosen from endometrium, thymus, spleen and parathyroid. The method can be used for normal tissue ablation, where the tissue is chosen from bone marrow and spleen. The disease or disorder is an autoimmune disease such as myasthenia gravis, lupus nephritis, lupus erythematosus, and rheumatoid arthritis, Class III autoimmune diseases such as immune-mediated thrombocytopenias, such as acute idiopathic thrombocytopenic purpura and chronic idiopathic thrombocytopenic purpura, dermatomyositis, Sjogren's syndrome, multiple sclerosis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcal nephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, sarcoidosis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitis ubiterans, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, polychondritis, pemphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis, or fibrosing alveolitis. The infectious disease is chosen from bacterial, fungal, parasitic and viral lesion. The infectious disease is caused by a fungus chosen from Microsporum, Trichophyton, Epidermophyton, Sporothrix schenckii, Cyrptococcus neoformans, Coccidioides immitis, Histoplasma capsulatum, Blastomyces dermatitidis, and Candida albicans. The infectious disease is caused by a virus chosen from HIV, herpes virus, cytomegalovirus, rabies virus, influenza virus, hepatitis B virus, Sendai virus, feline leukemia

virus, Reo virus, polio virus, human serum parvo-like virus, simian virus 40, respiratory syncytial virus, mouse mammary tumor virus, Varicella-Zoster virus, Dengue virus, rubella virus, measles virus, adenovirus, human T-cell leukemia viruses, Epstein-Barr virus, murine leukemia virus, mumps virus, vesicular stomatitis virus, Sindbis virus, lymphocytic choriomeningitis virus, wart virus and blue tongue virus. The infectious disease is caused by a bacterium chosen from Bacillus anthracis, Streptococcus agalactiae, Legionella pneumophilia, Streptococcus pyogenes, Escherichia coli, Neisseria gonorrhoeae, Neisseria meningitidis, Pneumococcus, Hemophilus influenzae B, Treponema pallidum, Lyme disease spirochetes, Pseudomonas aeruginosa, Mycobacterium leprae, Brucella abortus, Mycobacterium tuberculosis, and Tetanus toxin. The infectious disease is caused by a protozoa chosen from Plasmodium falciparum, Plasmodium vivax, Toxoplasma gondii, Trypanosoma rangeli, Trypanosoma cruzi, Trypanosoma rhodesiensei, Trypanosoma brucei, Schistosoma mansoni, Schistosoma japanicum, Babesia bovis, Elmeria tenella, Onchocerca volvulus, Leishmania tropica, Trichinella spiralis, Onchocerca volvulus, Theileria parva, Taenia hydatigena, Taenia ovis, Taenia saginata, Echinococcus granulosus, and Mesocestoides corti. The infectious disease is caused by a mycoplasma chosen from Mycoplasma arthritidis, M. hyorhinis, M. orale, M. arginini, Acholeplasma laidlawii, M. salivarum and M. pneumoniae. The cancer is preferably chosen from carcinoembryonic antigen (CEA)-expressing tumor or a CD20-expressing malignancy. The CD20-expressing malignancy is a B-cell lymphoma or leukemia (claimed).

Dwg.0/0

FS CPI EPI

FA AB; DCN

MC CPI: A10-E01; A12-V; A12-V01; A12-V03C2; B04-C03; B04-G01; B04-H01; B04-L05C; B05-A03A; B05-A03B; B05-A04; B05-B02A3; B05-C07; B06-A02; B06-A03; B06-F03; B07-A02B; B07-D13; B10-B01B; B10-B02A; B10-D03; B11-C07A; B12-K04A; B14-A01; B14-A02; B14-A03; B14-C06; B14-C09B; B14-F02D; B14-F03; B14-F04; B14-F07; B14-H01A; B14-H01B; B14-J01A4; B14-N10; B14-N11; B14-N12; B14-N14; B14-N15; B14-N17C; B14-S01; B14-S04; C04-C03; C04-G01; C04-H01; C04-L05C; C05-A03A; C05-A03B; C05-A04; C05-B02A3; C05-C07; C06-A02; C06-A03; C06-F03; C07-A02B; C07-D13; C10-B01B; C10-B02A; C10-D03; C11-C07A; C12-K04A; C14-A01; C14-A02; C14-A03; C14-C06; C14-C09B; C14-F02D; C14-F03; C14-F04; C14-F07; C14-H01A; C14-H01B; C14-J01A4; C14-N10; C14-N11; C14-N12; C14-N14; C14-N15; C14-N17C; C14-S01; C14-S04; D05-A01A4; D05-A01B3; D05-H09; D05-H11; K08-X; K09-B

EPI: S03-E09E; S03-E14H4

TECH UPTX: 20040505

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The antigen is chosen from carcinoembryonic antigen (CEA), HER-2/neu, epidermal growth factor receptor (EGFR), vascular endothelial growth factor (VEGF), placental growth factor (PLGF), tenascin, EGP-1, EGP-2, CD19, CD20, CD22, CD21, CD23, CD30, CD33, CD45, CD80 and CD74, alpha-fetoprotein, A3, CA125, colon-specific antigen-p (CSAp), folate receptor, human leukocyte antigen (HLA)-DR, human chorionic gonadotropin, Ia, interleukin (IL)-2, insulin-like growth factor, KS-1, Le(y), MAGE, MUC1, MUC2, MUC3, MUC4, NCA66, necrosis antigens, PAM-4, prostatic acid phosphatase (PAP), Pr1, prostate specific antigen (PSA), PSMA, S100, T101, TAC, IL-6 and TAG-72. The polymer conjugate has a general formula comprising (polymer backbone)-(agent)m, where m is an integer. The polymer conjugate further comprises a recognition hapten conjugated to the polymer. The polymer conjugate optionally has a general formula comprising (recognition hapten)n-(polymer backbone)-(agent)m, where n and m are integers. The recognition hapten is chosen from diethylenetriaminepentaacetic acid (DTPA), a metal complex of DTPA, 1,4,7,10-tetrazacyclododecane-N-N', N''', N'''-tetraacetic acid (DOTA), a metal complex of DOTA, N,N'-di(2-hydroxy-5-(ethylene-3-carboxy)benzyl)ethylenediamine N,N'-diacetic acid (HBED), a metal complex of HBED, fluorescein,

2,4-dinitrophenyl-derivatives, biotin and histaminyl-succinyl-glycine. The multi-specific antibody or antibody fragment is radiolabeled with a radionuclide chosen from **F-18**, P-32, Sc-47, Cu-62, Cu-64, Cu-67, Ga-67, Ga-68, Y-86, Y-90, etc. The method further comprises administering a clearing composition to the tissue and allowing the clearing composition to clear unbound multi-specific antibody or antibody fragment from the tissue. The multi-specific antibody or antibody fragment is a chimeric, humanized, or human monoclonal antibody. The polymer is chosen from polymers of single amino acids, co-polymers of two amino acids, co-polymers of three amino acids, co-polymers of four amino acids, polyethylene glycol (PEG), derivatives of PEG, co-polymers of PEG, N-(2-hydroxypropyl)methacrylamide (HPMA), polystyrene-co-maleic acid/anhydride (SMA), polyvinylether maleic anhydride (DIVEMA), polyethyleneimine, ethoxylated polyethyleneimine, starburst dendrimers, polyvinylpyrrolidone (PVP), apometallothionein and calicheamicin. The therapeutic agent is chosen from therapeutic radioisotope, toxin, cytokine, immunomodulator, drug, prodrug and boron addend. The drug is chosen from taxanes, nitrogen mustards, ethylenimine derivatives, alkyl sulfonates, nitrosoureas, triazenes; folic acid analogs, pyrimidine analogs, purine analogs, vinca alkaloids, antibiotics, enzymes, etc. The therapeutic or diagnostic agent is chosen from radioisotopes, enhancing agents for use in magnetic resonance imaging, contrasting agents, and coloring agents. The cytokine is chosen from IL-1, IL-2, IL-3, IL-6, IL-10, IL-12, IL-18, IL-21, interferon-alpha, interferon-beta, interferon-gamma, granulocyte macrophage-colony stimulating factor (GM-CSF), G-CSF, erythropoietin and thrombopoietin. In the photodynamic diagnosis or treatment method, the therapeutic agent is a photosensitizer such as dihematoporphyrin, benzoporphyrin monoacid ring A, tin etiopurpurin sulfonated aluminum phthalocyanine and lutetium texaphyrin.

ABEX UPTX: 20040505

WIDER DISCLOSURE - (1) targeting an agent towards a target site in tissue by administering multi-specific antibody as described above, and then administering a polymer conjugate; and
(2) a kit useful for target site in tissue or tissue sample.

L47 ANSWER 2 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1999-228967** [19] WPIX
DNC **C1999-067344**
TI Radiolabeling thiol-containing peptides with **fluorine**-18.
DC B04 D16 K08
IN **GRIFFITHS, G L**
PA (IMMU-N) **IMMUNOMEDICS INC**
CYC 83
PI WO 9911590 A1 19990311 (199919)* EN 22 C07B059-00 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9893756 A 19990322 (199931)
EP 1009726 A1 20000621 (200033) EN C07B059-00 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 6187284 B1 20010213 (200111) A61K051-00 <--
JP 2001515843 W 20010925 (200170) 25 C07K001-13 <--
US 6358489 B1 20020319 (200224) A61K051-00 <--
US 2002119096 A1 20020829 (200259) A61K051-00 <--
ADT WO 9911590 A1 WO 1998-US18268 19980903; AU 9893756 A AU 1998-93756 19980903; EP 1009726 A1 EP 1998-946820 19980903, WO 1998-US18268 19980903; US 6187284 B1 **Provisional US 1997-57485P 19970903**, US 1998-146318 19980903; JP 2001515843 W WO 1998-US18268 19980903, JP 2000-508634 19980903; US 6358489 B1 **Provisional US 1997-57485P 19970903**, Div ex US 1998-146318 19980903, US 2000-644706 20000824; US

2002119096 A1 **Provisional US 1997-57485P 19970903**, Div ex US 1998-146318 19980903, Div ex US 2000-644706 20000824, US 2002-71247 20020211

FDT AU 9893756 A Based on WO 9911590; EP 1009726 A1 Based on WO 9911590; JP 2001515843 W Based on WO 9911590; US 6358489 B1 Div ex US 6187284; US 2002119096 A1 Div ex US 6187284, Div ex US 6358489

PRAI **US 1997-57485P 19970903**; US 1998-146318 19980903; US 2000-644706 20000824; US 2002-71247 20020211

IC ICM **A61K051-00**; **C07B059-00**; **C07K001-13**
ICS A61K039-395; **A61K051-08**; **C07B039-00**; **C07K007-06**; **C07K016-00**; **C07K016-46**

AB WO 9911590 A UPAB: 19990518
NOVELTY - Simple efficient method for incorporating **18F** radionuclide into peptide-containing targeting vectors for use in clinical positron emission tomography.

DETAILED DESCRIPTION - Radiolabeling thiol-containing peptides with **fluorine**-18 comprising reacting a peptide comprising a free thiol group with a labeling reagent of formula (I) or a **fluorinated** alkene (II) in which at least one of the two double bonded carbon atoms bears at least one leaving group comprising I, Br, Cl, azide, tosylate, mesylate, nosylate or triflate.

n, m = 0-2;

n+m = 0-2;

X = I, Br, Cl, azide, tosylate, mesylate, nosylate, triflate, maleimide (optionally substituted by 1-2 alkyl) or 3-sulfomaleimide;

R1, R2 = I, Br, Cl, azide, tosylate, mesylate, nosylate, triflate, H, CONH2, COOH, OH, sulfonic acid, tertiary amine, quaternary ammonium, alkyl (optionally substituted by CONH2, COOH, OH, sulfonic acid, tertiary amine or quaternary ammonium), COOR', CONR'2 or COR'; and

R' = 1-6C alkyl or phenyl.

An INDEPENDENT CLAIM is included for the detection of tissue comprising:

(a) administration of a bispecific antibody or antibody fragment comprising an arm which is specific for a target tissue of the patient and another arm which is specific for an **F18** labeled peptide or a low molecular weight hapten conjugated to the **F18** labeled peptide and allowing the bispecific antibody or antibody fragment to bind to the target tissue and the non-targeted bispecific antibody or antibody fragment to clear;

(b) administration of the **F18**-labeled peptide or hapten conjugate to the patient and allowing the **F18**-labeled peptide or the hapten conjugate to bind to the specific antibody or antibody fragment and the unbound **F18**-labeled peptide or hapten conjugate to clear; and

(c) detecting the **F18**-labeled peptide, detecting the target tissue.

ACTIVITY - Diagnostics; Radionuclides.

MECHANISM OF ACTION - None given.

USE - For Radiolabeling peptide-containing targeting vectors such as proteins, antibodies, antibody fragments and receptor-targeted peptides for use in routine clinical positron emission tomography.

ADVANTAGE - The method is simple and efficient. The method uses the unique property of the free thiol groups which are rapidly alkylated at neutral pH and moderate temperature.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: **B04-C01B**; B11-C07A3; B12-K04B; D05-H09; D05-H11; D05-H12E; K08-X

TECH UPTX: 19990510
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred peptide: The peptide comprises a thiol group and preferably comprises F(ab')2, F(ab)2. Rab' or

Fab antibody fragments, single chain antibody subfragments, divalent antibody fragment constructs or antibody constructs comprising IgG3 or IgG3-F(ab')2 frameworks. The peptide is especially X-Gly-D-Tyr-D-Trp-Gly-D-Lys(X)-Gly-D-Tyr-D-Trp-OH, Ac-Cys(Y)-D-Tyr-D-Tro-Gly-D-Cys(Y)-Gly-D-Tyr-D-Trp-PH or Ac-Gly-D-iodo-Tyr-D-Trp-Gly-D-Lys(Ac)-Gly-D-iodo-Tyr-D-Tro-OH: X, Y = an optionally protected thiol group. The antibody fragment is preferably monoclonal, particularly humanized.
Preferred Hapten: The hapten is a metal chelate complex, preferably comprising manganese, iron or gadolinium.
Preferred Label: (I) comprises
18FCI3,
18FCHI2,
18FCHICOOCH2,
18FCI2COOH,
18FCI2COOMe,
18FCI2CH2OH,
18FCHICH2OH,
18CI2CH2COOH,
18CI2CH2N+(Me)3,
18FI2CH2-maleimide,
18CHICONH2,
18FCI2CONH2,
18GCHIO2Me,
18FCI2CO2Me,
18CHBr2,
18FCBr2CH2CH2SO3H,
18FCBr2CH2OH,
CF3COCI218F,
CH3COBr218F,
18FCHBrCN,
18FCI2CHCN,
CBrF218F, or
18FCBr(CONH2)2, preferably
18FCH2CI2COOH, or
18FCH2CI2CONH2.
(II) comprises:
18FCH=CI2,
18FCI=CH2, or
18CI=CI2.
Preferred Method: The **F18** labeled peptide is detected by positron emission tomography.

ABEX UPTX: 19990510

EXAMPLE - 1 mg lyophilized Fab'SH-NP (an anticarcinoembryonic antigen antibody fragment) is reconstituted with 1ml solution of 18FCI2COOH in 0.1M sodium acetate buffer at pH 6 for 30 minutes at room temperature. An aliquot of the mixture is analyzed to reveal that the antibody's hinge-region thiol groups effect nucleophilic displacement of both iodine atoms of 18FCI2COOH and the reaction proceeds in near quantitative yield. The **F18** labeled Fab' fragment is ready for injection.

DEFINITIONS - At least one of R1 and R2 is I; X = I

L47 ANSWER 3 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1999-101008** [09] WPIX
DNN **N1999-074010** DNC **C1999-030117**
TI Fluorescence labelling substance for amino acid containing substance - comprises fluorescent substance and reactive base.
DC B04 B05 S03
PA (AISE) AISIN SEIKI KK
CYC 1
PI JP 10330299 A 19981215 (199909)* 6 C07C022-04
ADT JP 10330299 A **JP 1997-155824 19970528**
PRAI **JP 1997-155824 19970528**

IC ICM C07C022-04
ICS **C07K001-13**; C07K002-00; G01N021-78; G01N033-533
AB JP 10330299 A UPAB: 19990302
Fluorescence labelling substance for amino acid containing substance comprises fluorescent substance and a reactive base which binds to a side chain of an amino acid in an amino acid containing substance. Also claimed is labelling of an amino acid containing substance by reacting fluorescence labelling substance with amino acid containing substance at at least pH 7.

The amount of fluorescence labelling substance to amino acid containing substance is preferably 0.25-0.5 mol equivalents. Amino acid containing substance is an amino acid, peptide, protein or antibody. Side chain of amino acid is amino base, hydroxyl base or thiol base. The reactive base is a halogen such as **F**, Cl, Br or I, isothiocyanate, carboxysuccinimidyl ester or maleimide. A linker is present between the fluorescent substance and a reactive base. The linker contains > 3C atoms. The fluorescent substance is an aromatic compound which emits fluorescence. Fluorescent substance is pyrene, coumarin, fluorescein, rhodamine, anthracene, fluorene, fluoranthene and/or cyanine compound. The fluorescence labelling substance and amino acid containing substance are reacted at -89 to 5 deg. C.

USE - The fluorescence labelling substance with high sensitivity and efficiency is used to label amino acid containing substance.
Dwg.0/2
FS CPI EPI
FA AB; DCN
MC CPI: B04-C01; B04-G01; B04-N04; B06-A01; B06-A03; B08-C02; B08-D03; B10-B02; B11-C07B3; B12-K04E
EPI: S03-E04E; S03-E14H4

L47 ANSWER 4 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1999-046951** [05] WPIX
DNC **C1999-014924**
TI New cyclic peptides inhibit ligand binding to integrins - used for tumour imaging and to treat e.g. thrombosis, myocardial infarct, arteriosclerosis, inflammation, stroke, angina, tumours, osteoporosis, ulcerative colitis and Crohn's disease.
DC B04 K08
IN DIEFENBACH, B; HAUBNER, R; JONCZYK, A; SCHWAIGER, M
PA (MERE) MERCK PATENT GMBH
CYC 1
PI DE 19725368 A1 19981217 (199905)* 13 C07K005-12 <--
ADT DE 19725368 A1 **DE 1997-1025368 19970616**
PRAI **DE 1997-19725368 19970616**
IC ICM **C07K005-12**
ICS A61K038-08; **C07K001-22**
AB DE 19725368 A UPAB: 19990203
Cyclic peptides of formula (I) are new. cyclo(Arg-Gly-Asp-D-E) (I) D, E = optionally derivatised amino acids selected from Gly, Ala, beta -Ala, Asn, Asp, Asp(OA), Arg, Cha, Cys, Gln, Glu, His, Ile, Leu, Lys, Lys(Ac), Lys(AcNH2), Lys(AcSH), Lys(R), Met, Nal, Nle, Orn, Phe, Phe(4-OA), Phe(4-Hal), homoPhe, Phg, Pro, Pya, Ser, Thr, Tia, Tic, Trp, Tyr, Tyr(3-I), Tyr(3-F) and Val; A = 1-18C alkyl; Hal = F, Cl, Br or I; Ac = optionally partially fluorinated 1-10C alkanoyl, 7-11C aroyl or 8-12C aralkanoyl; and R = chelator for radioactive isotopes. (I) can be alkylated on the N-atom of the peptide linkage and/or labelled at any position with 125-I, 123-I, 3-H, 11-C, 14-C, **18-F**, 15-O or other radioactive isotopes and chiral amino acids or amino acid derivatives can be in the L or D form.

USE - (I) are selective inhibitors of ligand binding to integrins. (I) can be used for tumour imaging, as affinity ligands for purifying integrins and as integrin inhibitors for treating e.g. circulatory disorders, thrombosis, myocardial infarct, arteriosclerosis,

inflammations, stroke, angina, tumours, osteoporosis, angiogenesis-related diseases, ulcerative colitis, Crohn's disease, psoriasis and postangioplastic restensosis and to enhance wound healing in microbial infections and acute kidney failure.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: **B04-C01A**; B11-C07B5; B12-K04A1; B14-C03; B14-E08; B14-E10C; B14-F01; B14-F02; B14-F04; B14-F07; B14-H01; B14-L06; B14-N01; B14-N16; B14-N17; K08-X; K09-B

L47 ANSWER 5 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1997-077233 [07] WPIX
CR 1999-276948 [23]; 2000-532867 [48]; 2001-588789 [66]; 2003-531036 [50]; 2004-141464 [14]
DNN N1997-064162 DNC C1997-024755
TI Contrast agent or targeted compsn. for imaging or treating diseased tissue - comprising lipid, protein or polymer, a gas, and a targeting ligand e.g. a protein, peptide, saccharide or steroid.
DC A18 A28 A96 B04 B05 D16 P31
IN SHEN, D; UNGER, E C; WU, G
PA (IMAR-N) IMARX PHARM CORP; (IMAR-N) IMARX PHARM INC
CYC 23
PI WO 9640285 A1 19961219 (199707)* EN 175 A61K049-00 <--
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN JP US
AU 9662703 A 19961230 (199716) <--
EP 831932 A1 19980401 (199817) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 11507638 W 19990706 (199937) 211 A61K045-00
AU 709562 B 19990902 (199948)
CN 1187137 A 19980708 (200336) A61K049-00
CN 1397348 A 20030219 (200337) A61K049-06
EP 831932 B1 20040506 (200430) EN A61K049-18
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 69632401 E 20040609 (200438) A61K049-18
EP 1444991 A1 20040811 (200452) EN A61K051-04
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1083280 C 20020424 (200519) A61K049-00
ADT WO 9640285 A1 **WO 1996-US9938 19960606**; AU 9662703 A **AU 1996-62703 19960606**; EP 831932 A1 **EP 1996-921486 19960606, WO 1996-US9938 19960606**; JP 11507638 W **WO 1996-US9938 19960606, JP 1997-502099 19960606**; AU 709562 B **AU 1996-62703 19960606**; CN 1187137 A **CN 1996-194499 19960606, WO 1996-US9938 19960606**; CN 1397348 A **Div ex CN 1996-194499 19960606, CN 2002-105309 19960606**; EP 831932 B1 **EP 1996-921486 19960606, WO 1996-US9938 19960606**; DE 69632401 E **DE 1996-632401 19960606, EP 1996-921486 19960606, WO 1996-US9938 19960606**; EP 1444991 A1 **Div ex EP 1996-921486 19960606, EP 2004-76279 19960606**; CN 1083280 C **CN 1996-194499 19960606**
FDT AU 9662703 A Based on WO 9640285; EP 831932 A1 Based on WO 9640285; JP 11507638 W Based on WO 9640285; AU 709562 B Previous Publ. AU 9662703, Based on WO 9640285; CN 1187137 A Based on WO 9640285; EP 831932 B1 Based on WO 9640285; DE 69632401 E Based on EP 831932, Based on WO 9640285; EP 1444991 A1 Div ex EP 831932
PRAI **US 1996-640464 19960501; US 1995-497684 19950607**
REP US 5209720; US 5362478; US 5380519
IC ICM A61K045-00; A61K049-00; A61K049-06; A61K049-18; A61K051-04
ICS A61B005-055; A61K031-74; A61K038-00; A61K038-08; A61K038-12; A61K047-48; A61K049-04; **A61K051-08**; A61K051-12; A61P007-02; C08F222-00; C08F226-00; C08G059-00; C08G069-00

ICA C08F220-44; C08G065-32
AB WO 9640285 A UPAB: 20050321
A contrast agent for diagnostic imaging or a target compsn. comprises: (i) a lipid, protein or polymer and (ii) a gas, in combination with (iii) a targeting ligand (T1). T1 targets cells or receptors selected from myocardial, endothelial, epithelial and tumour cells and the glycoprotein GPIIb/IIIa receptor. Also claimed are: a compsn. comprising vesicles containing (i) - (iii) and an aqueous carrier; a targeted vesicle compsn. comprising a **fluorinated** gas and a targeting ligand (T1') which targets tissues or receptors; a formulation for therapeutic or diagnostic use comprising (i)-(iii) and a bioactive agent; and a method for providing an image of an internal region of a patient, or for diagnosing the presence of diseased tissue, comprising: (a) admin of a compsn. as above; and (b) scanning the patient using ultrasound to obtain a visible image of the region or diseased tissue. Certain targeting cpds. are also claimed as new.

USE - The methods and cpds. are useful for imaging or diagnosing the presence of diseased tissue, especially myocardial, endothelial or epithelial tissue but also gastrointestinal and cardiovascular regions. In partic. the ligand targets regions of arteriosclerosis, especially atherosclerotic plaque or infarcted myocardium. Stabilised vesicles are partic. useful for perfusion imaging. The vesicles may also be used to deliver active agents to an intended target such as tissue or a receptor, and ultrasound can then be used to promote rupture of the vesicles and release a bioactive or diagnostic agent.

Dwg.0/0
FS CPI GMPI
FA AB; DCN
MC CPI: A12-V03C2; B04-B01B; B04-C03; B04-F01; B05-B01P; B12-K04; B12-K07; D05-H09

L47 ANSWER 6 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1990-163872** [21] WPIX
CR 1993-196269 [24]
DNC **C1990-071461**
TI Potentiation of biocidal activity - of amphiphilic ion channel-forming peptide(s), by co-admin. of toxic anion, and test for peptide(s) involving fluoride ion.
DC B04
IN STEINBERG, W H; ZASLOFF, M
PA (MAGA-N) MAGAININ SCI INC; (CHIL-N) CHILDRENS HOSPITAL PHILADELPHIA; (MAGA-N) MAGAININ SCIENCES I
CYC 28
PI

WO 9004408	A	19900503 (199021)*				<--
RW: AT BE CH DE FR GB IT LU NL SE						
W: AU BG BR DK FI HU JP KR NO RO SU						
PT 92078	A	19900430 (199022)				<--
CA 2001150	A	19900421 (199023)				<--
AU 8945028	A	19900514 (199031)				<--
ZA 8907935	A	19901228 (199105)				<--
CN 1043263	A	19900627 (199113)				<--
NO 9101470	A	19910415 (199131)				<--
EP 441832	A	19910821 (199134)				<--
R: AT BE CH DE FR GB IT LI LU NL SE						
DK 9100715	A	19910621 (199137)				<--
HU 57992	T	19920128 (199209)				<--
ES 2024729	A	19920301 (199214)				<--
JP 04502904	W	19920528 (199228)		6	A61K037-02	<--
AU 641129	B	19930916 (199344)			A61K037-02	<--
IL 92061	A	19940125 (199413)			A61K037-00	<--
EP 441832	B1	19940615 (199423)	EN	11	A61K037-02	<--
R: AT BE CH DE FR GB IT LI LU NL SE						
DE 68916261	E	19940721 (199429)			A61K037-02	<--

EP 441832 A4 19921028 (199524) <--
ADT ZA 8907935 A **ZA 1989-7935 19891019**; EP 441832 A **EP 1989-912164 19891018**; JP 04502904 W **JP 1989-511302 19891018**, **WO 1989-US4664 19891018**; AU 641129 B **AU 1989-45028 19891018**; IL 92061 A **IL 1989-92061 19891020**; EP 441832 B1 **EP 1989-912164 19891018**, **WO 1989-US4664 19891018**; DE 68916261 E **DE 1989-616261 19891018**, **EP 1989-912164 19891018**, **WO 1989-US4664 19891018**; EP 441832 A4 EP 1989-912164
FDT JP 04502904 W Based on WO 9004408; AU 641129 B Previous Publ. AU 8945028, Based on WO 9004408; EP 441832 B1 Based on WO 9004408; DE 68916261 E Based on EP 441832, Based on WO 9004408
PRAI **US 1988-261237 19881021**; **US 1989-353618 19890518**
REP US 4507230; WO 8806597
IC ICM A61K037-02
ICS A61K033-02; A61K033-16; A61K033-20; A61K033-40; **C07K007-08**; **C07K007-10**; C12Q001-04; G01N033-68
AB WO 9004408 A UPAB: 19940803
(A) To inhibit growth of a target cell in a host there are administered (a) at least one biologically active, ion channel-forming amphiphilic peptide and/or protein, and (b) a toxic anion. A compsn. comprises (a9 and (b). (B) To test an unknown sample for the presence of ion channel-forming peptides, a first portion of the sample is contacted with a first sample of target cells and the biological activity is measured against the cells; a second portion of the sample and a . given amount of fluoride ion are contacted with a second sample of target cells containing the same type of cells as the first sample, and the biological activity of the second portion and the fluoride ion is measured against the cells; and the two measured activities are compared to determine the presence of channel-forming peptides in the sample. If the second portion has greater biological activity against the target cells than does the first portion, then the sample contains ion channel-forming peptides or proteins. Pref. the target cell is a bacterium.
USE - Components (a) and (b) may be administered as a single compsn. or in separate compsns., which compsns. may contain conventional additives. The anion potentiates the action of the peptide or protein. The latter are used at dosages of 1-500 mg/kg when administered systemically or at concns. of 0.05-5% when used topically. Respective figures for the anion are 1-10 mg/kg and 0.05-2%. The combination may have anti-tumour, anti-microbial, anti-viral or anti-parasitic use. It may be used for oral hygiene. @(27pp Dwg.No.0/0)
0/0
FS CPI
FA AB; DCN
MC CPI: B04-B02B1; B04-B04A; **B04-C01**; B05-C04; B05-C07; B05-C08; B11-C08E; B12-A01; B12-A02C; B12-A06; B12-B04; B12-G07; B12-K04A
ABEQ EP 441832 B UPAB: 19940727
A composition comprising: (a) at least one biologically active amphiphilic peptide and/or biologically active protein, said peptide or protein being an ion channel-forming peptide or protein; and (b) a toxic anion.
Dwg.0/0

L47 ANSWER 7 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1990-007315** [01] WPIX
TI New radio-halogenated amino phenol derivs. and antibody conjugates - useful therapeutically and for in vivo or in vitro diagnosis.
DC B05 K08
IN ALVAREZ, V L; BELINKA, B A; COUGHLIN, D J
PA (CYTO-N) CYTOGEN CORP
CYC 17
PI WO 8911876 A 19891214 (199001)* EN 49 <--
RW: AT BE CH DE ES FR GB GR IT LI LU NL SE

EP 348261 A 19891227 (199001) EN <--
W: AU JP
AU 8937728 A 19900105 (199012) <--
US 4966999 A 19901030 (199046) <--
JP 02504643 W 19901227 (199107) <--
CA 1318615 C 19930601 (199327) C07C243-38 <--
EP 348261 B1 19931215 (199350) EN 31 C07C243-00 <--
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 68911397 E 19940127 (199405) C07C243-00 <--
ES 2062061 T3 19941216 (199505) C07C243-00 <--

ADT WO 8911876 A **WO 1989-US2467 19890606**; EP 348261 A **EP 1989-401557 19890606**; US 4966999 A **US 1988-203793 19880607**; JP 02504643 W **JP 1989-506891 19890606**; CA 1318615 C **CA 1989-601795 19890605**; EP 348261 B1 **EP 1989-401557 19890606**; DE 68911397 E **DE 1989-611397 19890606, EP 1989-401557 19890606**; ES 2062061 T3 **EP 1989-401557 19890606**

FDT DE 68911397 E Based on EP 348261; ES 2062061 T3 Based on EP 348261

PRAI **US 1988-203793 19880607**

REP US 2808416; US 3809721; US 4430319; 2.Jnl.Ref; EP 203764; US 3979506

IC A61K039-39; A61K043-00; A61K049-02; **C07B059-00**; C07C091-30; C07C093-04; C07C109-10; C07C215-76; **C07K015-00**

ICM C07C243-38

ICS A61K039-39; A61K043-00; A61K047-48; A61K049-02; **C07B059-00**; C07C091-30; C07C093-04; C07C109-10; C07C215-76; C07C217-00; **C07K015-00**

AB WO 8911876 A UPAB: 19930928
Radiohalogenated amino phenol derivative of formula (I) are new, where R1 = H, alkyl, or hydroalkyl, R2 = acid hydrazide, alkyl acid hydrazide, hydrazino, alkylhydrazine, alkylphenylhydrazine, alkylamine or alkoxyamine, R3 = H, alkyl or R2, R4 = alkyl, hydroxyalkyl or R2 and X1 = radioactive isotope of F, Br, I or Atomic Also new are radiohalogenated antibody conjugates comprising (I) attached via a covalent bond between th amino of (I) and an oxidised carbohydrate moiety of an antibody or antibody fragment in which the oxidised carbohydrate moiety is not part of nor directly involved with the antigen binding region, the amine of the conjugate is derived from a reactive amine of (I) from hydrazino, hydrazine, phenylhydrazine, phenylhydrazine, alkylhydrazine and alkoxyhydrazine and in which the conjugate is characterised by, (a) the same immunospecificity as the unconjugated antibody or antibody fragment, and (b) aqueous solubility such athat it is suitable for in vivo admin.
USE/ADVANTAGE - (I) are useful in preparation of the antibody conjugates useful for a variety of in vivo therapeutic and diagnostic applications as well as for in vito diagnostic methods.
0/5

FS CPI

FA AB; DCN

MC CPI: B04-B04C; B05-A04; K09-B; K09-E

ABEQ US 4966999 A UPAB: 19930928
Radiohalogenated cpds. are of formula (I), in which R1 = H, alkyl or hydroxyalkyl, R2 = acid hydrazide, alkyl acid hydrazine, hydrazino, alkylhydrazine, alkylphenylhydrazine, alkylamine or alkoxyamine, R3 = H, alkyl or R2, R4 = alkyl, hydroxyalkyl or R2 and X is a radioactive isotope of I, Br, F and As.
USE/ADVANTAGE - Useful as intermediates for prepg. radiohalogenated antibody conjugates.

ABEQ EP 348261 B UPAB: 19940203
A compound of the formula (I) in which R1 = H, alkyl or hydroxyalkyl; R2 = acid hydrazide, alkyl acid hydrazide, hydrazino, alkylhydrazine, alkylphenylhydrazine, alkylamine or alkoxyamine,; R3 = H, alkyl or R2; R4 = alkyl, hydroxyalkyl or R2; and X = a radioactive isotope of iodine, bromine, fluorine or astatine.
Dwg.0/4

L47 ANSWER 8 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1988-309158** [44] WPIX
DNC **C1988-136708**
TI New radio halogenated alkene derivs. - useful for labelling protein cpds..
DC B04 K08
IN HADLEY, S W; WILBUR, D S
PA (NEOR-N) NEORX CORP
CYC 7

PI	EP 289187	A	19881102 (198844)*	EN	21		<--
	AU 8814658	A	19881020 (198850)				<--
	NO 8801635	A	19881107 (198850)				<--
	DK 8802088	A	19881017 (198902)				<--
	JP 01034930	A	19890206 (198911)				<--
	US 4870188	A	19890926 (198948)		9		<--
	CN 1030748	A	19890201 (198951)				<--
	US 4876081	A	19891024 (199001)		15		<--
	US 5200169	A	19930406 (199316)		14	C07D207-46	<--
	CA 1338770	C	19961203 (199708)			C07K001-13	<--

ADT EP 289187 A **EP 1988-303474 19880418**; JP 01034930 A **JP 1988-94405 19880416**; US 4870188 A **US 1987-39155 19870416**; US 4876081 A **US 1988-171731 19880405**; US 5200169 A **CIP of US 1987-39155 19870416, Div ex US 1988-171731 19880405, US 1989-350104 19890705**; CA 1338770 C **CA 1988-564230 19880415**
FDT US 5200169 A CIP of US 4870188, Div ex US 4876081
PRAI **US 1987-39155 19870416; US 1988-171731 19880405**
REP 5.Jnl.Ref; A3...9013; No-SR.Pub; US 4450149
IC ICM C07D207-46; **C07K001-13**
ICS A61K037-02; A61K039-44; A61K043-00; A61K049-02; **A61K051-08**; **C07B059-00**; C07C021-02; C07C057-52; C07C063-74; C07C069-62; C07C069-65; C07C069-76; C07C103-62; C07F003-10; C07F005-02; C07F007-22; **C07K003-08**; **C07K015-12**; G01N033-53
AB EP 289187 A UPAB: 19930923
Radiohalogenated alkene derivs. of formula (I) and (II) are new: In (I) and (II), X = radiohalogen; R1 and R2 = (a) H, (b) opt. substd. alkyl, provided that any sp2 or sp C atom substd. on the alkyl gp. is separated from C=C by at least one fully substd. sp3 C atom, (c) opt. substd. aryl, (d) C-bonded heteroalkyl, provides that any sp2 or sp C atom bonded to a heteroatom is not conjugated with C=C and that any single sp3 C atom intervening between such an sp2 or sp C atom and C=C must be fully substd. (e) heteroaryl, provided that no heteroatom is bonded to or conjugated with C=C, or (f) a mixed alkyl aryl gp., provided that no heteroatom is bonded to C=C, an aryl gp. is bonded directly to C=C or is separated from it by at least one sp3 C atom, and any single sp3 C atom between C=C and an aryl gp. must be fully substd. Y is a gp. of type (b)-(f) bearing a functional gp. capable of reacting with a protein, protein fragment or polypeptide without affecting its biological activity.
USE - (I) and (II) are useful for introducing radiohalogen into monoclonal antibodies, plasma proteins, peptides, etc., for diagnostic and therapeutic purposes.
0/3
FS CPI
FA AB
MC CPI: B05-A02; B05-A03A; B05-A03B; B05-A04; B05-B01A; B05-B01B; B12-K04; K09-B; K09-E
ABEQ US 4870188 A UPAB: 19930923
The tetrafluorophenyl ester of 5-X-4-pentenoic acid, the tetrafluorophenyl ester of 3,3-dimethyl-5-X-4-pentenoic acid, the tetrafluorophenyl ester of 4-(2'-X-ethenyl)benzoic acid, the N-succinimidyl ester of 5-X-4-pentenoic acid, the N-succinimidyl ester of 3,3-dimethyl-5-X-4-pentenoic acid and the N-succinimidyl ester of 4-(2'-X-ethenyl)benzoic acid are new. In the cpds. X is a radiohalogen.

Pref. X is 123I, 124I, 125I, 131I, 75Br, 76Br, 77Br, **18F** or 211At.

USE/ADVANTAGE - The radiohalogenated cpds. are useful for coupling to proteins, esp. monoclonal antibodies, to provide reagents for diagnostic and therapeutic applications.

ABEQ US 4876081 A UPAB: 19930923
Radiohalogenoethylene derivs. of formula X-C(R)=C(R')-y and/or RR'C=C(Y)-X are new. In these formulae, X is a radioactive halogen nucleide; R and R' are each H, opt. substd. alkyl, opt. substd. aryl, heterocyclylalkyl, heterocyclylaryl or aralkyl, such that the sp2 hybrid character of the double bond system is retained; and Y is defined as R or R', but is not H and is or contains a substit. capable of coupling with a protein, protein fragment or a without significant loss of biological acitivity.

USE - These derivs. are coupled with biologically active proteins, protein fragments or polypiptides to obtain radioactive diagnostic reagents and therapeutics.

ABEQ US 5200169 A UPAB: 19930923
Vinyl derivs. of formula (I) or (II) are new.

In the formula X is a radiohalogen; R1 and R2 are each H, 1-12C alkyl, or 5-7C aryl; Y is benzoic acid bonded to an activated functional gp. to facilitate bonding of the cpd. to polypeptides, proteins and protein fragments under conditions that preserve the biological activity of the polypeptides, proteins and protein fragments, the functional gp being an imide ester, alkylimide ester, amidoalkyl imide ester, succinimide ester, acylsuccinimide, imidate ester, alkyl imidate ester, amidoalkylimidate ester, phenolic ester, (opt substd), or tetra fluorophenyl ester. Alkyl is 1-12C. X is pref. 123I, 125I, 131I, 75B, 77Br, **18F** on 211 At.

USE/ADVANTAGE - (I) can be coupled to proteins such as monoclonal antibodies to provide diagnostic and therapeutic reagents., 0/0

L47 ANSWER 9 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1988-264287** [37] WPIX
CR 1985-177615 [29]; 1985-310116 [49]; 1986-055415 [08]; 1986-131364 [20]; 1987-306724 [43]; 1988-021391 [03]; 1988-119308 [17]; 1994-056365 [07]
DNC **C1988-117705**
TI Introducing radioactive fluorine into peptide(s) and drugs - by reaction with 4-bromo methyl-benzoyl derivative, then exchange of bromo with fluoro, especially for making imaging agents for brain scanning.
DC B05 K08
IN FURLANO, D C; JACOBSON, K A; KIRK, K L
PA (USSH) US DEPT HEALTH & HUMAN SERVICE
CYC 1
PI US 168494 A0 19880802 (198837)* 33 <--
US 5098996 A 19920324 (199215) 13 <--
ADT US 168494 A0 **US 1988-168494 19880315**; US 5098996 A **US 1988-168494 19880315**
PRAI **US 1988-168494 19880315**; **US 1983-717624 19830324**; **US 1984-664953 19841026**; **US 1986-833035 19860226**; **US 1986-874143 19860613**
IC A61K000-01; C07D473-06; C07H019-16; **C07K001-02**; **C07K007-40**
AB US N7168494 N UPAB: 20011211
Fluorine, especially **18-F**, is introduced into peptides and functionalised drugs by (i) coupling a p-bromomethylbenzoyl (BMB) gp. to an amino gp. in the peptide etc., via its N-hydroxy-succinimide ester (or by other standard methods of activation), then (2) reacting the product with Bu4N+F- (e.g. in MeCN) or with KF-'Kryptofix' to replace the Br with F, forming a p-fluoromethyl-benzoyl (FMB) gp.

Alternatively, a functionalised BMB gp.is fluorinated first, then the product reacted with the drug, biopolymer, etc.

USE/ADVANTAGE - Products containing **18F** are useful in diagnostic nuclear medicine, eg. as imaging agents in the brain (using positron-emission tomography scanning). The process for introducing F is generally applicable and rapid.
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-A04; B11-C07B5; B12-K04B; K09-B; K09-E
ABEQ US 5098996 A UPAB: 19930923
Fluorinated cpds. and **18F** radiotracers are made from NH2-contg. cpds. by (a) coupling a p-bromoethyl benzoyl-contg. cpd. of NH2-cpd. cpd.; and (b) fluorinating prod. to substitute Br with F to form prod.
Coupling is through an N-hydroxysuccinimide ester, and NH2-contg. cpd. is an aminoacid or peptide. Reaction is conducted in a non-reactive polar aprotic solvent.
USE - In diagnostic nuclear medicine.

L47 ANSWER 10 OF 10 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1986-320680 [49] WPIX
DNC C1986-138640
TI Radio halogenated small molecules for protein labelling - especially of monoclonal antibodies specific for tumour antigens.
DC B04 D16 K08
IN FRITZBERG, A R; JONES, D S; WILBUR, D S
PA (NEOR-N) NEORX CORP
CYC 16

PI	EP 203764	A	19861203 (198649)*	EN	26	<--
	R: AT BE CH DE FR GB IT LI LU NL SE					
	NO 8601962	A	19861215 (198705)			<--
	DK 8602269	A	19861118 (198707)			<--
	JP 62277331	A	19871202 (198803)			<--
	CN 86108331	A	19871104 (198846)			<--
	US 4885153	A	19891205 (199006)			<--
	US 5045303	A	19910903 (199138)			<--
	EP 203764	B1	19930324 (199312)	EN	21 C07B059-00	<--
	R: AT BE CH DE FR GB IT LI LU NL SE					
	DE 3688103	G	19930429 (199318)		C07B059-00	<--
	US 5213787	A	19930525 (199322)		6 A61K043-00	<--
	JP 08143490	A	19960604 (199632)		13 C07C025-02	<--
	US 5609848	A	19970311 (199716)		13 A61K051-02	<--
	JP 09194406	A	19970729 (199740)		13 C07C025-02	<--
	JP 09208507	A	19970812 (199742)		13 C07C025-02	<--

ADT EP 203764 A **EP 1986-303757 19860516**; JP 62277331 A **JP 1986-136324 19860613**; US 4885153 A **US 1989-338497 19890413**; US 5045303 A **US 1987-137952 19871223**; EP 203764 B1 **EP 1986-303757 19860516**; DE 3688103 G **DE 1986-3688103 19860516**, **EP 1986-303757 19860516**; US 5213787 A **Cont of US 1985-735392 19850517, Cont of US 1987-137952 19871223, US 1990-627806 19901212**; JP 08143490 A **JP 1995-130844 19950529**; US 5609848 A **Cont of US 1985-735392 19850517, Cont of US 1987-137952 19871223, Cont of US 1989-333394 19890405, Cont of US 1989-388864 19890803, US 1991-764001 19910923**; JP 09194406 A **Div ex JP 1995-130844 19860613, JP 1996-324419 19860613**; JP 09208507 A **Div ex JP 1986-136324 19860613, JP 1996-218888 19860613**
FDT DE 3688103 G Based on EP 203764; US 5213787 A Cont of US 5045303; US 5609848 A Cont of US 5045303
PRAI **US 1986-852740 19860421; US 1985-735392 19850517; US 1987-137952 19871223; US 1990-627806 19901212; US 1989-333394 19890405; US 1989-388864 19890803; US 1991-764001 19910923**
REP 4.Jnl.Ref; A3...9013; DE 2497500; EP 11858; No-SR.Pub; US 3979506;

3.Jnl.Ref; DE 2947500

IC ICM A61K043-00; **A61K051-02**; **C07B059-00**; C07C025-02
ICS A61K037-04; A61K038-16; A61K039-39; A61K049-02; **A61K051-00**; C07C017-20; C07C025-18; C07C047-55; C07C057-00; C07C057-60; C07C067-307; C07C069-65; C07C069-76; C07C211-52; C07C233-00; C07C233-64; C07C233-65; C07C243-22; C07C319-12; C07C323-09; C07C331-28; C07D207-40; C07D521-00; C07F003-12; **C07K001-13**; **C07K014-00**; **C07K015-00**; G01N033-534; G01N033-58; G01N033-60; G01N033-68

ICA A61K035-16; A61K038-00; A61K039-395; C07C057-58; C07C257-08; C07F007-22; C07F015-00

ICI C07M005:00

AB EP 203764 A UPAB: 19970417
Radiohalogenated small molecule cpds. of formula X'-Ar-R (I) and organometallic intermediates of formula M-Ar-R (IV) are new: X' = a radio isotope of iodine, bromine, **fluorine** or astatine; Ar = aromatic or heteroaromatic ring; R = a short-chain substit. that does not highly activate the ring onto which the radioisotope is substd. and that bears a functional gp. suitable for conjugation to protein, whilst preserving the biological activity of the protein; M = Sn(n-Bu)3, SnMe3, HgX2, Hg(OAC)2, B(OH)2 or BZ3; X = Cl, Br or I; Z = alkyl or alkoxy.

USE/ADVANTAGE - (I) are useful for labelling proteins, particularly antibodies, which are then used for clinical diagnosis and therapy. Substd. of the radiohalogen onto a non-activated aromatic ring provides a radiolabelled protein with greater stability than prior art substns. onto activated aromatic rings such as phenols. Monoclonal antibodies radiolabelled with (I) show enhanced in vivo stability. (I) are especially useful for labelling antibodies specifically reactive with tumour cell associated antigens.

Dwg.0/4

FS CPI

FA AB

MC CPI: B05-A02; B05-A03A; B05-A04; B05-B01A; B12-K04A1; D05-H10; K09-B; K09-E

ABEQ EP 203764 B UPAB: 19930922
A compound having the general formula X-Ar-R wherein X represents a radioisotope of iodine, bromine, **fluorine** or astatine; Ar is aromatic or heteroaromatic ring; and R is a short-chain substituent comprising a phenolic ester, imideester, imidate ester, anhydride acrylsuccinimide, aldehyde, isothiocyanate, thiol, diazo, hyrazine, alkyl halide, maleimide, alkyl imide ester, amido alkyl imide ester, alkyl imidate ester, or amido alkyl imidiate ester that does not highly activate the ring onto which the radioisotope is substituted and has a functional group suitable for conjugation to protein under conditions that preserve the biological activity of the protein.

0/4

ABEQ US 4885153 A UPAB: 19930922
New pure radiohalogenated protein is prod. by covalently linking protein and cpd. A=Ar-R where Ar is aromatic or heteroaromatic ring; R is bond or 1-12C substit. that does not activate Ar to electrophillic substitn. as by OH or NH2 substitn.; the bond or substit. has a functional gp. attached to covalently link to protein preserving its biological activity, e.g. phenolic, imide or imidate ester, anhydride, acylsuccinimide, aldehyde, isothiocyanate, thiol diazo, amine, hydrazine, alkyl, halide or maleimide; X (asterisk): is radioisotope of I, Br, F or mastatine and is m- or p- to R.

USE - Radiohalogenate protein may be prod. e.g. by metallating with haloaryl cpds. with functional gp. with Sn(n-Bu)3, or SnMe3, then transmetallizing site specifically with

organometallic gp., e.g. Hghalo, Hg(OAc)2, Bhalo, B(alkyl or alkoxy)3, and subsequent radiohalogenation by demetallation. The functional gp. is then conjugated to protein, e.g. monoclonal antibody, SE-labelled antibiotics, for diagnosis or therapy, e.g. tumour imaging and

radiotherapy. Fig (I) shows biodistribution.

ABEQ US 5045303 A UPAB: 19930922

A new compsn. of high Sp. activity comprises a non-radioactive cpd. of formula X-Ar-R and a cpd. of formula X(star)-Ar-R where Ar is an aromatic ring; R is a bond or substit. contg. 1-12 straight chain C that does not activate Ar to electrophilic substitn. of same order as does OH of NH2, and the bond or substitn. carries a functional gp. suitable for covalent linkage to protein without degrading the biological activity of the protein (e.g. by acylation). Functional gps. include phenolic ester, anhydride, acylsuccinimide, imide ester, imidate ester aldehyde, isothiocyanate, diazo, hydrazine, alkyl halide, and maleimide; X(star) is radioisotope of I, Br, F, At, and is p- or m-positioned.

Pref. X(star) is 123I, 125I, 131I, 75Br, 76Br, or 211At and pref. R is alkylimideamido alkylimide-, imidate-, alkyl imidate-, or amido alkylimidate-ester. Typical cpds. include N-succinimidyl 3(4'-(X(star)halophenyl)propionate. Radiohalogenating a protein comprises reacting its NH2, SH or OH-gps. in aq. soln. with above cpd.

USE/ADVANTAGE - Radiolabelling of monoclonal antibodies, antigens, hormones, etc. in a stable way with good yield and high Sp. activity for diagnosis and therapy, esp. of cancer. @

ABEQ US 5213787 A UPAB: 19931115

New compsns. comprise a non-radioactive cpd. of formula: X-Ar-R-NH2 and a cpd. of formula: X1-Ar-R-NH2. Ar = an aromatic ring. R = (CH2)n or CONH(CH2)n, (where n = 1-12) and does not activate Ar to electrophilic substitution of the order produced by OH or NH2 substitution of the ring. X1 is a radioisotope of I, Br, F or At and is p- or m-positioned relative to R. X is the non-radioactive form of X1. NH2 is a functional gp. suitable for covalent linkage to a protein udner conditions which preserve its biological activity.

Pref. X1 is 123I, 125I, 131I, 75Br, 76Br, 77Br, **18F** or 211At.

USE - For conjugation to proteins, e.g. monoclonal antibodies, for diagnosis and therapy, e.g. of cancer.

Dwg.0/0

ABEQ US 5609848 A UPAB: 19970417

A cpd. having the formula;

*X-Ar-R

wherein *X is a radioisotope of iodine, bromine, **fluorine**, or astatine; Ar is an aromatic ring; R is CONH (CH2)n; n is an integer between 0-12; where R has attached thereto a functional group Q suitable for conjugation to a protein under conditions that preserve the biological activity of the protein; and Q is an amine.

=> => fil reg
FILE 'REGISTRY' ENTERED AT 10:04:08 ON 19 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 APR 2005 HIGHEST RN 848724-42-5
DICTIONARY FILE UPDATES: 18 APR 2005 HIGHEST RN 848724-42-5

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from  *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l64
L61         2173 SEA FILE=REGISTRY ABB=ON  PLU=ON  18F/BI
L62              STR

F—G1—C—G1—A
1   2   3   4   5


REP G1=(0-2) CH2
NODE ATTRIBUTES:
NSPEC   IS RC     AT   5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   5

STEREO ATTRIBUTES: NONE
L64          915 SEA FILE=REGISTRY SUB=L61 SSS FUL L62

100.0% PROCESSED   2040 ITERATIONS                      915 ANSWERS
SEARCH TIME: 00.00.01


=> d his

     (FILE 'HOME' ENTERED AT 08:20:41 ON 19 APR 2005)
               SET COST OFF

     FILE 'WPIX' ENTERED AT 08:20:51 ON 19 APR 2005
L1            690 S C07B039/IPC
L2            523 S C07B059/IPC
L3            695 S (18F OR F18)/BIX
L4             21 S (18FLUORIN? OR 18 FLUORIN?)/BIX
                  E 18F/DCN
                  E 18F/SDCN
                  E 18F/CN
L5            212 S (18 F OR F 18)/BIX
                  E FLUORINE/DCN
                  E FLUORIDE/DCN
                  E E5+ALL
L6            650 S E2
L7           2212 S E6 OR 1777/DRN
L8             14 S E8
L9           4820 S L1-L8
L10          2668 S L9 AND PY<=1997
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L11        3114 S L9 AND PRY<=1997
L12        2953 S L9 AND AY<=1997
L13        3114 S L10-L12
L14          38 S L13 AND (B04-C01? OR C04-C01? OR B04-N01 OR B04-N02 OR B04-N0
L15          79 S L13 AND C07K/IPC
L16          15 S L13 AND A61K051-08/IPC
L17         140 S L13 AND A61K051/IPC
L18          20 S L13 AND C07K001-13/IPC
L19          24 S L16,L18
L20           2 S L19 AND ?FLUORI?/BIX
L21          22 S L19 NOT L20
                SEL DN AN 21
L22           1 S L21 AND E1-E2
L23          67 S L14,L15 NOT L19
                SEL DN AN 6 44 49 57
L24           4 S L23 AND E3-E9
L25          96 S L17 NOT L14-L16,L18-L24
                SEL DN AN 3 7 9 22 23 26 28 54
L26           8 S L25 AND E10-E25
                E GRIFFITHS G/AU
L27          75 S E3,E10,E11
                E IMMUNO/PA
                E IMMUNOMED/PA
L28         133 S E3-E6
L29         163 S L27,L28
L30          23 S L29 AND L9
                SEL DN AN 7 19
L31           2 S L30 AND E1-E5
L32           8 S L20,L22,L24,L31
L33         253 S C07K001-13/IPC
L34         343 S A61K051-08/IPC
L35         555 S L33,L34
L36         243 S L35 AND PY<=1997
L37         320 S L35 AND PRY<=1997
L38         318 S L35 AND AY<=1997
L39         325 S L36-L38
L40           6 S L39 AND ?FLUORI?/BIX
L41           3 S L39 AND L3-L8
L42           7 S L40,L41
                SEL DN AN 2 4 5
L43           4 S L42 NOT E6-E12
L44           9 S L32,L43
L45          21 S L39 AND F/BIX NOT L40-L44
                SEL DN AN 4
L46           1 S L45 AND E13-E15
L47          10 S L44,L46 AND L1-L46

     FILE 'WPIX' ENTERED AT 09:26:42 ON 19 APR 2005
L48        1198 S L1,L2
L49         937 S L48 AND L13
L50          67 S L49 AND C07K/IPC
L51          15 S L49 AND A61K051-08/IPC
L52          68 S L50,L51
L53           4 S L52 AND ?FLUORI?/BIX
L54           3 S L3-L8 AND L52
L55           3 S 18F?/BIX AND L52
L56           5 S L53-L55
L57          13 S L52 AND F/BIX
L58          10 S L56,L57 NOT L47

     FILE 'HCAPLUS' ENTERED AT 09:32:19 ON 19 APR 2005
L59           1 S US20020119096/PN
                SEL RN
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     FILE 'REGISTRY' ENTERED AT 09:32:32 ON 19 APR 2005
L60           37 S E16-E52
                 E 18F
L61         2173 S E3
L62              STR
L63           35 S L62 SAM SUB=L61
L64          915 S L62 FUL SUB=L61
                 SAV L64 NEON071/A
L65           24 S L60 AND L64

     FILE 'HCAPLUS' ENTERED AT 09:35:48 ON 19 APR 2005
L66         1597 S L64
L67          720 S L66 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L68            1 S L66 AND GRIFFITHS ?/AU
L69            1 S L66 AND IMMUNOMED?/PA,CS
L70            1 S L68,L69,L59
L71           13 S L67 AND (PROTEIN? OR PEPTIDE? OR AMINO ACID?)/SC,SX
L72           22 S L67 AND (PROTEIN? OR PEPTIDE? OR AMINO(L)ACID?)/CT,CW
L73           52 S L67 AND (?PROTEIN? OR ?PEPTIDE? OR AMINOACID OR AMINO ACID)
L74            5 S L71-L73 AND FLUORIN?/CW
L75            1 S L71-L73 AND HALOGEN?/CW
L76            6 S L74,L75
L77            6 S L70,L76
L78           56 S L71-L73 NOT L77
                 SEL HIT RN L77
                 SEL HIT RN L78

     FILE 'REGISTRY' ENTERED AT 09:43:51 ON 19 APR 2005
L79           40 S E1-E40
L80           64 S E41-E104
L81           16 S L79 NOT L60
L82            1 S L81 AND C9H11FO3S
L83           59 S L80 NOT L60,L79
L84            4 S L83 AND (C2H4FI OR C4H8FI OR C3H6FI OR C3H6BRF)
L85            5 S L82,L84

     FILE 'HCAPLUS' ENTERED AT 09:49:15 ON 19 APR 2005
L86           58 S L85
L87           17 S L86 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L88           18 S L70,L87
L89            4 S L88 AND (PROTEIN? OR PEPTIDE? OR AMINO(L)ACID?)/CT,CW,SX,SC
L90            3 S L88 AND ?PROTEIN?
L91            2 S L88 AND ?PEPTIDE?
L92            0 S L88 AND AMINOACID
L93            3 S L88 AND FLUORINATION+OLD,NT,PFT,RT/CT
L94           68 S L67 AND FLUORINATION+OLD,NT,PFT,RT/CT
L95            1 S L94 AND THIOL
L96            5 S L89-L93,L95,L70
L97           13 S L88 NOT L96
L98           13 S L88 AND 8/SC,SX
L99           15 S L96,L98
L100           3 S L88 NOT L99

     FILE 'REGISTRY' ENTERED AT 10:04:08 ON 19 APR 2005

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FILE COVERS 1907 - 19 Apr 2005 VOL 142 ISS 17
FILE LAST UPDATED: 18 Apr 2005 (20050418/ED)

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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d l99 all hitstr tot

L99 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:184209 HCAPLUS
DN 130:206780
ED Entered STN: 22 Mar 1999
TI Fluorination of **proteins** and **peptides** for F-18
positron emission tomography
IN **Griffiths, Gary L.**
PA **Immunomedics, Inc., USA**
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07B059-00
ICS A61K051-08; C07K001-13
CC **8-1** (Radiation Biochemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9911590	A1	19990311	WO 1998-US18268	19980903	<--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2302360	AA	19990311	CA 1998-2302360	19980903	<--
	AU 9893756	A1	19990322	AU 1998-93756	19980903	<--
	EP 1009726	A1	20000621	EP 1998-946820	19980903	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	US 6187284	B1	20010213	US 1998-146318	19980903	<--
	JP 2001515843	T2	20010925	JP 2000-508634	19980903	<--
	US 6358489	B1	20020319	US 2000-644706	20000824	<--
	US 2002119096	A1	20020829	US 2002-71247	20020211	<--
PRAI	US 1997-57485P	P	19970903	<--		
	US 1998-146318	A3	19980903			
	WO 1998-US18268	W	19980903			
	US 2000-644706	A3	20000824			

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

WO 9911590	ICM	C07B059-00	
	ICS	A61K051-08; C07K001-13	
WO 9911590	ECLA	A61K051/08; A61K051/10; C07B059/00K; C07K001/107D4; C07K001/13; C07K016/30A; C07K016/46D	<--
US 6187284	ECLA	A61K051/08; A61K051/10; C07K016/30A; C07K016/46D	<--
US 6358489	ECLA	A61K051/08; A61K051/10; C07B059/00K; C07K001/107D4; C07K001/13; C07K016/30A; C07K016/46D	<--
US 2002119096	ECLA	A61K051/08; A61K051/10; C07B059/00K; C07K001/107D4; C07K001/13; C07K016/30A; C07K016/46D	<--

OS MARPAT 130:206780

AB **Thiol**-containing **peptides** can be radiolabeled with fluorine-18 (F-18) by reacting a **peptide** comprising a free **thiol** group with an F-18-bound labeling reagent which also has a group that is reactive with **thiols.** The labeling reagent has the general formula 18F-(CH2)m-CR1R2-(CH2)n-X, where n = 0, 1 or 2; m = 0, 1 or 2; and n + m = 0, 1 or 2. X is selected from a group including halides, azide, tosylate, maleimides, etc. R1 and R2 are the same or different and may be, among others, a halide, triflate, hydroxyl, alkyl. The resulting F-18-labeled **peptides** may be targeted to a tissue of interest using bispecific antibodies or bispecific antibody fragments having one arm specific for the F-18-labeled **peptide** or a low mol. weight hapten conjugated to the F-18-labeled **peptide**, and another arm specific to the targeted tissue. The targeted tissue is subsequently visualized by clin. positron emission tomog.

ST fluorine 18 labeling **protein peptide** PET

IT Immunoglobulins
RL: SPN (Synthetic preparation); PREP (Preparation)
(G3, radiolabeled; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT Carcinoembryonic antigen
RL: MSC (Miscellaneous)
(antibody fragment to; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT Haptens
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(conjugates with radiopharmaceuticals; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT Drug targeting
Fluorination
Positron-emission tomography
Radiopharmaceuticals
(fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT Reagents
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT Immunoglobulins
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(fragments, for radiolabeling and targeted radiopharmaceuticals; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(humanized, for targeted radiopharmaceuticals; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT Antibodies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(monoclonal, for targeted radiopharmaceuticals; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT Antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(single chain, radiolabeled; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT **Peptides, reactions**
Proteins, specific or class
RL: RCT (Reactant); RACT (Reactant or reagent)
(**thiol** group-containing; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT 7439-89-6D, Iron, complexes conjugated with radiopharmaceuticals, biological studies 7439-96-5D, Manganese, complexes conjugated with radiopharmaceuticals, biological studies 7440-54-2D, Gadolinium, complexes conjugated with radiopharmaceuticals, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT **220934-28-1P 220934-29-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT 9034-40-6DP, LH-RH, radiolabeled cysteine derivative 220934-30-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT **220934-31-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT 181224-33-9 **220934-32-7 220934-33-8**
220934-34-9 220934-35-0 220934-36-1
220934-37-2 220934-38-3 220934-39-4
220934-40-7 220934-41-8 220934-42-9
220934-43-0 220934-44-1 220934-45-2
220934-46-3 220934-47-4 220934-48-5
220934-49-6 220934-50-9 220934-51-0
220934-52-1 220934-53-2 220934-54-3D, iodinated
RL: RCT (Reactant); RACT (Reactant or reagent)
(labeling reagent; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

IT 75-47-8, Triiodomethane 594-68-3, Triiodoacetic acid 67862-54-8, Fluoride (18F1-) 91795-63-0 205652-45-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Immunomedics; WO 9816254 A 1998 HCAPLUS
(2) Kilbourn, M; JOURNAL OF NUCLEAR MEDICINE 1987, V28(4), P462 HCAPLUS
(3) Lang, L; APPLIED RADIATION AND ISOTOPES 1994, V45(12), P1155 HCAPLUS
(4) Page, R; NUCLEAR MEDICINE AND BIOLOGY 1994, V21(7), P911 HCAPLUS
(5) Shiue, C; JOURNAL OF LABELLED COMPOUNDS AND RADIOPHARMACEUTICALS 1989, V26, P287
(6) Vaidyanathan, G; BIOCONJUGATE CHEMISTRY 1994, V5, P352 HCAPLUS
(7) Vaidyanathan, G; NUCLEAR MEDICINE AND BIOLOGY 1995, V22(6), P759 HCAPLUS
(8) Wilbur, D; BIOCONJUGATE CHEMISTRY 1992, V3(6), P433 MEDLINE

(9) Zheng, L; JOURNAL OF NUCLEAR MEDICINE 1997, V38(5), P177P
IT **220934-28-1P 220934-29-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)
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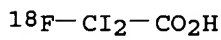
CN Acetic acid, fluoro-18F-diiodo- (9CI) (CA INDEX NAME)



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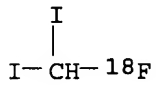
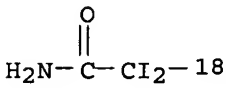
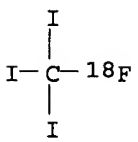
CN Methane, fluoro-18F-diiodo- (9CI) (CA INDEX NAME)



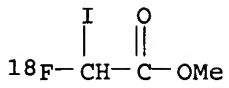
IT **220934-31-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)
RN 220934-31-6 HCAPLUS
CN Acetamide, 2-(fluoro-18F)-2,2-diiodo- (9CI) (CA INDEX NAME)



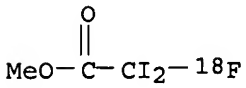
IT **220934-32-7 220934-33-8 220934-34-9**
220934-35-0 220934-36-1 220934-37-2
220934-38-3 220934-39-4 220934-40-7
220934-41-8 220934-42-9 220934-43-0
220934-44-1 220934-45-2 220934-46-3
220934-47-4 220934-48-5 220934-49-6
220934-50-9 220934-52-1 220934-53-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(labeling reagent; fluorination of **proteins** and **peptides** for F-18 positron emission tomog.)
RN 220934-32-7 HCAPLUS
CN Methane, fluoro-18F-triiodo- (9CI) (CA INDEX NAME)



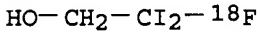
RN 220934-33-8 HCAPLUS
CN Acetic acid, fluoro-18F-iodo-, methyl ester (9CI) (CA INDEX NAME)



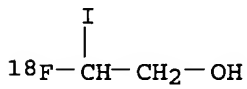
RN 220934-34-9 HCAPLUS
CN Acetic acid, fluoro-18F-diiodo-, methyl ester (9CI) (CA INDEX NAME)



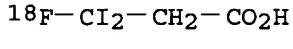
RN 220934-35-0 HCAPLUS
CN Ethanol, 2-(fluoro-18F)-2,2-diiodo- (9CI) (CA INDEX NAME)



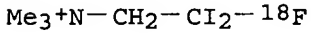
RN 220934-36-1 HCAPLUS
CN Ethanol, 2-(fluoro-18F)-2-iodo- (9CI) (CA INDEX NAME)



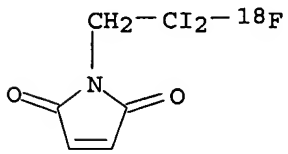
RN 220934-37-2 HCAPLUS
CN Propanoic acid, 3-(fluoro-18F)-3,3-diiodo- (9CI) (CA INDEX NAME)



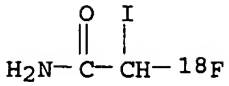
RN 220934-38-3 HCAPLUS
CN Ethanaminium, 2-(fluoro-18F)-2,2-diiodo-N,N,N-trimethyl- (9CI) (CA INDEX NAME)



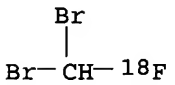
RN 220934-39-4 HCAPLUS
CN 1H-Pyrrole-2,5-dione, 1-[2-(fluoro-18F)-2,2-diiodoethyl]- (9CI) (CA INDEX NAME)



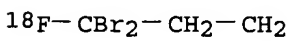
RN 220934-40-7 HCAPLUS
CN Acetamide, 2-(fluoro-18F)-2-iodo- (9CI) (CA INDEX NAME)



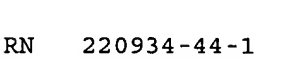
RN 220934-41-8 HCAPLUS
CN Methane, dibromofluoro-18F- (9CI) (CA INDEX NAME)



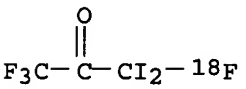
RN 220934-42-9 HCAPLUS
CN 1-Propanesulfonic acid, 3,3-dibromo-3-(fluoro-18F)- (9CI) (CA INDEX NAME)



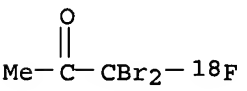
RN 220934-43-0 HCAPLUS
CN Ethanol, 2,2-dibromo-2-(fluoro-18F)- (9CI) (CA INDEX NAME)



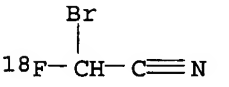
RN 220934-44-1 HCAPLUS
CN 2-Propanone, 1,1,1-trifluoro-3-(fluoro-18F)-3,3-diiodo- (9CI) (CA INDEX NAME)



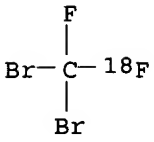
RN 220934-45-2 HCAPLUS
CN 2-Propanone, 1,1-dibromo-1-(fluoro-18F)- (9CI) (CA INDEX NAME)



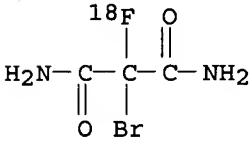
RN 220934-46-3 HCAPLUS
CN Acetonitrile, bromofluoro-18F- (9CI) (CA INDEX NAME)



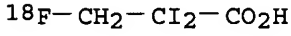
RN 220934-47-4 HCAPLUS
CN Methane, dibromofluorofluoro-18F- (9CI) (CA INDEX NAME)



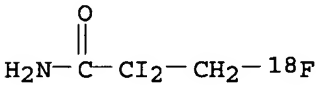
RN 220934-48-5 HCAPLUS
CN Propanediamide, 2-bromo-2-(fluoro-18F)- (9CI) (CA INDEX NAME)



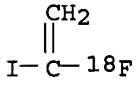
RN 220934-49-6 HCAPLUS
CN Propanoic acid, 3-(fluoro-18F)-2,2-diiodo- (9CI) (CA INDEX NAME)



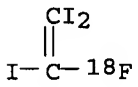
RN 220934-50-9 HCAPLUS
CN Propanamide, 3-(fluoro-18F)-2,2-diiodo- (9CI) (CA INDEX NAME)



RN 220934-52-1 HCAPLUS
CN Ethene, 1-(fluoro-18F)-1-iodo- (9CI) (CA INDEX NAME)



RN 220934-53-2 HCAPLUS
CN Ethene, fluoro-18F-triiodo- (9CI) (CA INDEX NAME)



L99 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:674101 HCAPLUS
DN 127:316325
ED Entered STN: 24 Oct 1997
TI [18F]β-CIT-FP is superior to [11C]β-CIT-FP for quantitation of the dopamine transporter
AU Lundkvist, Camilla; Halldin, Christer; Ginovart, Nathalie; Swahn, Carl-Gunnar; Farde, Lars
CS KAROLINSKA INSTITUTET, DEPARTMENT OF CLINICAL NEUROSCIENCE, PSYCHIATRY

SECTION, KAROLINSKA HOSPITAL, STOCKHOLM, S-17176, Swed.
SO Nuclear Medicine and Biology (**1997**), 24(7), 621-627
CODEN: NMBIEO; ISSN: 0969-8051
PB Elsevier
DT Journal
LA English
CC **8-9** (Radiation Biochemistry)
Section cross-reference(s): 27
AB β-CIT-FP [N-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl)nortropane] is a cocaine analog with high affinity for the dopamine transporter. Positron emission tomog. (PET) studies with [O-methyl-11C]β-CIT-FP ([11C]β-CIT-FP) has shown that equilibrium conditions were approached but, however, not reached at the end of measurement. Moreover, metabolite studies of [11C]β-CIT-FP in monkey plasma demonstrated a lipophilic-labeled metabolite that may enter the brain. We therefore labeled β-CIT-FP with fluorine-18 in a position that may avoid the formation of labeled lipophilic metabolites. The more long-lived radionuclide (18F) was used to allow for measurements over longer time. [N-fluoropropyl-18F]β-CIT-FP ([18F]β-CIT-FP) was prepared by N-alkylation of nor-β-CIT with [18F]fluoropropyl bromide. PET studies were performed in cynomolgus monkeys. [18F]β-CIT-FP entered the brain rapidly. There was a high concentration of radioactivity in the striatum and much lower in the thalamus, neocortex, and cerebellum. The striatum-to-cerebellum ratio was about 5 at time of transient equilibrium, which occurred after 60 to 100 min. After pretreatment with GBR 12909, radioactivity in the striatum was markedly reduced, thus indicating specific [18F]β-CIT-FP binding to the dopamine transporter. The fraction of unchanged [18F]β-CIT-FP determined by HPLC was 10-15% after 140 min. No lipophilic labeled metabolites were detected. The absence of measurable lipophilic labeled metabolites and the occurrence of transient equilibrium within the time of the PET measurement indicate that [18F]β-CIT-FP is superior to [11C]β-CIT-FP as a PET radioligand for quantification of the dopamine transporter in the human brain.
ST fluorine 18 CIT FP dopamine transporter; brain dopamine transporter PET radioligand
IT Brain
Positron-emission tomography
([18F]β-CIT-FP vs. [11C]β-CIT-FP for quantitation of dopamine transporter in brain)
IT Transport **proteins**
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(dopamine-transporting; [18F]β-CIT-FP vs. [11C]β-CIT-FP for quantitation of dopamine transporter in brain)
IT 186381-69-1P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
([18F]β-CIT-FP vs. [11C]β-CIT-FP for quantitation of dopamine transporter in brain)
IT 172651-50-2
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
([18F]β-CIT-FP vs. [11C]β-CIT-FP for quantitation of dopamine transporter in brain)
IT 109-64-8, 1,3-Dibromopropane 136794-87-1
RL: RCT (Reactant); RACT (Reactant or reagent)
([18F]β-CIT-FP vs. [11C]β-CIT-FP for quantitation of dopamine transporter in brain)
IT **108607-98-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

([18F]β-CIT-FP vs. [11C]β-CIT-FP for quantitation of dopamine transporter in brain)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Baldwin, R; Nucl Med Biol 1995, V22, P211 HCAPLUS
(2) Bergstrom, K; (in press) Eur J Nucl Med
(3) Bergstrom, K; Hum Psychopharmacol 1996, V11, P483
(4) Boja, J; J Med Chem 1994, V37, P1220 HCAPLUS
(5) Chaly, T; Nucl Med Biol 1996, V23, P999 HCAPLUS
(6) Farde, L; J Cerebr Blood Flow Metab 1989, V9, P696 HCAPLUS
(7) Farde, L; Synapse 1994, V16, P93 HCAPLUS
(8) Halldin, C; Nucl Med Biol 1991, V18, P871 HCAPLUS
(9) Halldin, C; PET for Drug Development and Evaluation 1995, P55 HCAPLUS
(10) Halldin, C; Synapse 1996, V18, P871
(11) Karlsson, P; Psychopharmacology 1993, V113, P149 HCAPLUS
(12) Kuikka, J; Eur J Nucl Med 1995, V22, P356 MEDLINE
(13) Loc'H, C; J Label Compd Radiopharm 1995, V37, P64
(14) Lundkvist, C; J Label Compd Radiopharm 1995, V37, P52
(15) Lundkvist, C; J Nucl Med 1996, V37, P192
(16) Lundkvist, C; Nucl Med Biol 1995, V22, P905 HCAPLUS
(17) Marcusson, J; Brain Res 1988, V457, P122 HCAPLUS
(18) Neumeyer, J; J Med Chem 1994, V37, P1558 HCAPLUS
(19) Swahn, C; Hum Psychopharmacol 1994, V9, P25 HCAPLUS
(20) Swahn, C; J Label Compd Radiopharm 1996, V38, P675 HCAPLUS
(21) Wienard, K; J Comput Assist Tomogr 1994, V18, P110
(22) Wilson, A; Appl Radiat Isot 1995, V46, P765 HCAPLUS
(23) Wong, D; Synapse 1993, V15, P130 HCAPLUS

IT **108607-98-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

([18F]β-CIT-FP vs. [11C]β-CIT-FP for quantitation of dopamine transporter in brain)

RN 108607-98-3 HCAPLUS

CN Propane, 1-bromo-3-(fluoro-18F)- (9CI) (CA INDEX NAME)

L99 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:279058 HCAPLUS

DN 126:250893

ED Entered STN: 01 May 1997

TI Preparation of fluorine-18-labeled choline derivatives and their use as diagnostic agents for PET

IN Hara, Toshihiko; Kobayashi, Yoshiro; Izeki, Katsuhiko; Nagai, Takafumi

PA Daikin Ind Ltd, Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM C07C215-40
ICS A61K051-00; A61K049-00; C07B059-00; C07M005-00

CC 23-4 (Aliphatic Compounds)
Section cross-reference(s): 8

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09048747	A2	19970218	JP 1995-218052	19950803 <--
JP 2809145	B2	19981008		

PRAI JP 1995-218052 19950803 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 09048747	ICM	C07C215-40
	ICS	A61K051-00; A61K049-00; C07B059-00; C07M005-00

OS MARPAT 126:250893

AB RfMe2N+CH2CH2OH X- (I; Rf = fluoroalkyl, fluoroalkenyl, fluoroalkynyl, at least one F of these group is 18F; X- = conjugate base of acid) are prepared by treatment of RfX with Me2NCH2CH2OH. Diagnostic agents for PET, e.g. for diagnosis of cerebral tumor, containing I are also claimed. An MeCN solution of K2CO3 and Kryptofix 2,2,2 was added to an aqueous solution containing 18F-, and the solvent was evaporated from the mixture to give K18F, which was treated with an MeCN solution of 1,2-bis(tosyloxy)ethane at 80° for 20 min to give 18F-1-fluoro-2-(tosyloxy)ethane. This was further treated with Me2NCH2CH2OH at 80° for 30 min to give 18F-2-fluoroethyldimethyl-2-hydroxyethylammonium p-toluenesulfonate.

ST fluorine 18 labeled choline PET; imaging agent fluorine 18 choline

IT Positron-emission tomography
(computed; preparation of 18F-labeled choline derivs. as diagnostic imaging agents for PET)

IT Tomography
Tomography
(contrast agents; preparation of 18F-labeled choline derivs. as diagnostic imaging agents for PET)

IT Imaging agents
Imaging agents
(contrast, tomog.; preparation of 18F-labeled choline derivs. as diagnostic imaging agents for PET)

IT 13981-56-1, Fluorine-18, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(ion; preparation of 18F-labeled choline derivs. as diagnostic imaging agents for PET)

IT **113426-12-3P** 113426-14-5P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 18F-labeled choline derivs. as diagnostic imaging agents for PET)

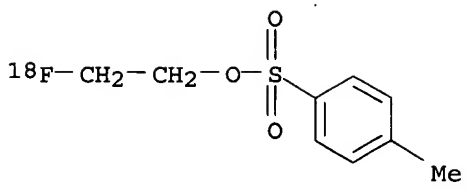
IT 188709-03-7P 188709-05-9P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 18F-labeled choline derivs. as diagnostic imaging agents for PET)

IT 108-01-0 5469-66-9, 1,3-Bis(tosyloxy)propane 6315-52-2, 1,2-Bis(tosyloxy)ethane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 18F-labeled choline derivs. as diagnostic imaging agents for PET)

IT **113426-12-3P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 18F-labeled choline derivs. as diagnostic imaging agents for PET)

RN 113426-12-3 HCAPLUS

CN Ethanol, 2-(fluoro-18F)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)



L99 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:334561 HCAPLUS
DN 125:80556
ED Entered STN: 08 Jun 1996
TI The carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine
AU Wester, Hans Juergen
CS Inst. Nuclearchem., Forschungszent. Juelich G.m.b.H., Juelich, D-52425, Germany
SO Berichte des Forschungszentrums Juelich (**1996**), Juel-3206, 1-157 pp.
CODEN: FJBEE5; ISSN: 0366-0885
DT Report
LA German
CC **8-1** (Radiation Biochemistry)
AB The nucleic properties of 18F for noninvasive diagnosis with positron emission tomog. (PET), 18F-fluorination procedures via prosthetic group labeling, and subsequent conjugation were investigated and compared with respect to synthesis time, radiochem. yield, suitability for automation, in vivo stability, and preservation of the biol. activity of the labeled biomols. Three methods were investigated: acylation by N-succinimidyl 4-[18F]fluorobenzoate ([18F]SFB), by nitrophenyl 2-[18F]fluoropropionate ([18F]NPFP), and photochem. conjugation by 4-azidophenayl [18F]fluoride ([18F]APF). Compared to [18F]APF, **protein** labeling with [18F]SFB gave rise to considerable radiochem. yield of up to 90%. The conjugation yields by [18F]NPFP in the presence of 1-hydroxybenzotriazole depend on the relative Lys, Tyr, and His content of the **proteins** used, whereas photochem. conjugation with [18F]APF, as well as acylation with [18F]SFB, predominantly depended on the Lys content. The applicability of these methods so smaller bioactive **peptides** was demonstrated. As a potential tracer for the cerebral amino acid transport system, O-(2[18F]fluoroethyl)-Tyr was prepared by O-2-[18F]fluoroethylation of fully protected Tyr and unprotected tyr by 2-[18F]fluoroethyltosylate with a radiochem. yield of 35-39%. The tracer showed high and continuous uptake in mice brain reaching 2.5% injected dose/g at 60 min and exhibited high in vivo stability.
ST fluorine 18 fluorination **protein peptide** tyrosine
IT Brain
(carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)
IT Avidins
Transferrins
RL: RCT (Reactant); RACT (Reactant or reagent)
(carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)
IT Albumins, biological studies
Amino acids, biological studies
Peptides, biological studies
Proteins, biological studies
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(carrier-free 18F-fluorination of **proteins**, **peptides**

, and tyrosine)

IT Immunoglobulins
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(G, carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)

IT Tomography
(positron-emission, carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine for potential PET)

IT **Fluorination**
(radiochem., carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)

IT 56-41-7, Alanine, biological studies 61-90-5, Leucine, biological studies 63-91-2, Phenylalanine, biological studies 70-78-0, 3-Iodotyrosine 672-87-7 6230-11-1 24250-85-9 51110-01-1, Somatostatin 65555-88-6
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)

IT 13981-56-1, Fluorine-18, biological studies
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)

IT 56-45-1, Serine, reactions 72-19-5, Threonine, reactions 583-52-8 584-08-7 2592-95-2 24345-16-2, Apamine 57018-46-9 **113426-12-3** 124915-06-6 159174-30-8 178432-96-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)

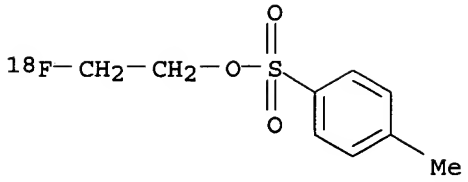
IT 50-99-7DP, D-(+)-Glucose, SMS 201-995 conjugates 59-23-4DP, D-(+)-Galactose, SMS 201-995 conjugates 63-42-3DP, SMS 201-995 conjugates 69-79-4DP, SMS 201-995 conjugates 619-84-1P 1109-28-0DP, D-Maltotriose, SMS 201-995 conjugates 4326-36-7P 10011-97-9P 14809-53-1DP, Yttrium 86, SDZ 215-811 complexes, preparation 15750-15-9DP, Indium 111, SMA 215-811 complexes, preparation 15757-14-9DP, Gallium 68, SDZ 216-927 complexes, preparation 83150-76-9DP, Sms 201-995, sugar conjugates 83150-76-9P, Sms 201-995 138661-02-6DP, SDZ 215-811, indium-111 and yttrium-86 complexes 147790-82-7DP, Sdz 216-927, gallium-68 complexes 178602-43-2P 178602-44-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)

IT 56-87-1P, L-Lysine, preparation 60-18-4P, Tyrosine, preparation 71-00-1P, Histidine, preparation 19121-31-4P, Hydrofluoric-18F acid 124915-09-9P 141762-27-8P 159174-29-5DP, human serum albumin conjugates 178273-73-9P 178432-97-8P 178432-98-9DP, IgG conjugates 178432-99-0P 178433-00-6P 178433-01-7P 178433-02-8P 178433-03-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)

IT **113426-12-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(carrier-free 18F-fluorination of **proteins**, **peptides**, and tyrosine)

RN 113426-12-3 HCAPLUS

CN Ethanol, 2-(fluoro-18F)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)

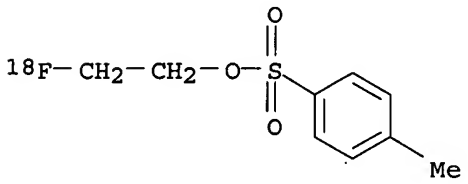


L99 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:507708 HCAPLUS
DN 122:260004
ED Entered STN: 25 Apr 1995
TI Synthesis of ω-fluoroalkoxy and alkoxy derivatives of raclopride: evaluation as radioligands for PET study of cerebral dopamine D2 receptors
AU Banks, William R.; Moerlein, Stephen M.; Parkinson, David; Welch, Michael J.
CS Edward Mallinckrodt Inst. Radiology, Washington Univ. School Medicine, Saint Louis, MO, 63110, USA
SO Medicinal Chemistry Research (**1995**), 5(2/3), 150-73
CODEN: MCREEB; ISSN: 1054-2523
PB Birkhaeuser
DT Journal
LA English
CC **8-9** (Radiation Biochemistry)
AB A series of analogs of the dopamine D2 receptor antagonist raclopride were evaluated as radiopharmaceuticals for positron emission tomog. (PET). In vitro assays indicate that the D2 affinity of the ligands are decreased by replacement of the 2-methoxy group of raclopride with ω-fluoroalkoxy substituents, and increased by removal of the 6-hydroxy substituent. The 2-fluoroethyl derivative of dehydroxyraclopride, [(S)-2-[(3,5-dichloro-2-(2'-fluoroethoxy)benzamido)-methyl]-1-(ethyl)pyrrolidine], exhibited a D2 affinity (Ki = 12 nM) close to that of raclopride itself (Ki = 9.5 nM). A one-step radiosynthesis of the fluorine-18 labeled analog of this ligand with specific radioactivity >2 Ci/μmol and 35% radiochem. yield (decay-corrected) was developed; there was poor receptor-specific localization of this radioligand in vivo in rats, however. These results underscore the inadequacy of in vitro receptor assays as the sole screening test for PET radiopharmaceuticals. Future development of this series of ligands should emphasize placement of the fluorine-18 label at an aromatic site remote from the intramol. hydrogen-bonding sites necessary for receptor-active conformations.
ST fluorine 18 fluoroalkoxy raclopride prepn; PET dopamine D2 receptor brain
IT Brain
(raclopride ω-fluoroalkoxy and alkoxy derivs. synthesis and evaluation as radioligands for PET of cerebral dopamine D2 receptors)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dopaminergic D2, raclopride ω-fluoroalkoxy and alkoxy derivs. synthesis and evaluation as radioligands for PET of cerebral dopamine D2 receptors)
IT Tomography
(positron-emission, raclopride ω-fluoroalkoxy and alkoxy derivs. synthesis and evaluation as radioligands for PET of cerebral dopamine D2 receptors)
IT 162760-93-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(raclopride ω-fluoroalkoxy and alkoxy derivs. synthesis and evaluation as radioligands for PET of cerebral dopamine D2 receptors)

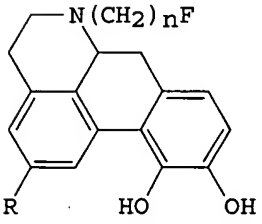
IT 320-72-9P 6315-52-2P 22775-37-7P 64122-23-2P 68276-69-7P
90348-73-5P **113426-12-3P** 162760-76-1P 162760-77-2P
162760-78-3P 162760-79-4P 162760-80-7P 162760-81-8P 162760-82-9P
162760-83-0P 162760-84-1P 162760-85-2P 162760-86-3P 162760-87-4P
162760-88-5P 162760-89-6P 162760-90-9P 162760-91-0P 162760-92-1P
162760-94-3P 162760-95-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(raclopride ω-fluoroalkoxy and alkoxy derivs. synthesis and evaluation as radioligands for PET of cerebral dopamine D2 receptors)

IT **113426-12-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(raclopride ω-fluoroalkoxy and alkoxy derivs. synthesis and evaluation as radioligands for PET of cerebral dopamine D2 receptors)

RN 113426-12-3 HCAPLUS
CN Ethanol, 2-(fluoro-18F)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)



L99 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:490220 HCAPLUS
DN 119:90220
ED Entered STN: 04 Sep 1993
TI Synthesis and in vivo distribution in the rat of several fluorine-18 labeled N-fluoroalkylaporphines
AU Zijlstra, S.; Visser, G. M.; Korf, J.; Vaalburg, W.
CS PET Cent., Univ. Groningen, Groningen, 9713, Neth.
SO Applied Radiation and Isotopes (**1993**), 44(4), 651-8
CODEN: ARISEF; ISSN: 0883-2889
DT Journal
LA English
CC **8-9** (Radiation Biochemistry)
Section cross-reference(s): 31
GI



I, R=H, n=2
II, R=H, n=3
III, R=HO, n=3

AB A method is described for the rapid production and purification of new potential
dopamine agonists. Via microwave heating 10,11-dihydroxy-N-(2-fluoroethyl)norapomorphine (I), 10,11-dihydroxy-N-(3-

fluoropropyl)norapomorphine (II) and 2,10,11-trihydroxy-N-(3-fluoropropyl)norapomorphine (III) and their isotopic fluorine-18 derivs. were synthesized. The fluorine-18 label was introduced via N-fluoroalkylation of acylated noraporphine derivs. with no-carrier-added (n.c.a.) 18F(CH2)2I and 18F(CH2)3I. Within 160 min (E.O.B.), radiochem. yields of 13-29% (corrected for decay) were achieved based on [18F]fluoroalkyliodide. The specific activity obtained, ranged from 15 to 75 GBq/μmol. The fluorine-18 labeled compds. were investigated for their in vivo binding potency to the D2-receptors. After i.v. injection, the distribution was studied in rats. High uptakes of the N-[18F]fluoroalkylaporphines were found in the lungs, liver, adrenals and kidneys. No significant different radioactive accumulation was observed in striatum, cerebellum and frontal cortex. Dopamine depletion with reserpine did not affect the striatum to cerebellum ratio at low dosage of N-[18F]fluoroalkylaporphines (10 nmol/kg).

ST fluorine 18 fluoroalkylaporphine tissue distribution prepn; aporphine fluorine 18 tissue distribution prepn

IT Adrenal gland, metabolism
Blood
Blood plasma
Bone, metabolism
Brain, metabolism
Heart, metabolism
Kidney, metabolism
Liver, metabolism
Lung, metabolism
Muscle, metabolism
Spleen, metabolism
(fluorine-18-labeled fluoroalkylaporphines distribution in, dopaminergic agonist activity in relation to)

IT Neurotransmitter agonists
(dopaminergic, hydroxy(fluoroalkyl)norapomorphines, preparation and in vivo distribution of)

IT 762-51-6, 2-Fluoroethyl iodide
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of acetoxynorapomorphine derivs.)

IT 6315-52-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(fluorine-18-labeled substitution reaction of)

IT 149156-26-3 149156-27-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(fluoroalkylation of, microwave-induced)

IT 149156-24-1P 149180-58-5P 149180-59-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deacetylation of)

IT 149156-28-5P 149156-29-6P 149180-60-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and in vivo tissue distribution of, dopamine agonist activity in relation to)

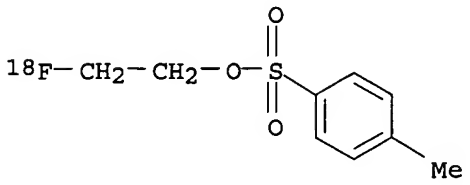
IT 67862-54-8P, Fluoride (18F1-)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and substitution reactions of)

IT 146578-65-6P 146578-67-8P 149156-25-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as dopamine agonist)

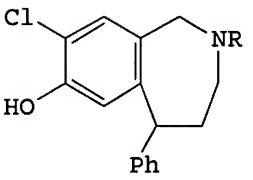
IT **113426-12-3** 113426-14-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with acetoxynorapomorphines)

IT **113426-12-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with acetoxynorapomorphines)

RN 113426-12-3 HCAPLUS
CN Ethanol, 2-(fluoro-18F)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)



L99 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:181404 HCAPLUS
DN 114:181404
ED Entered STN: 17 May 1991
TI The utility of 1-[18F]fluoro-3-iodopropane for the synthesis of certain dopamine D-1 and benzodiazepine receptor radioligands
AU Teng, Ren Rui; Bai, Lan Qin; Shiue, Chyng Yann; Dewey, Stephen L.; Arnett, Carroll D.; Wolf, Alfred P.; Hitzemann, Robert J.
CS Chem. Dep., Brookhaven Natl. Lab., Upton, NY, 11973, USA
SO Nuclear Medicine and Biology (**1990**), 17(8), 811-17
CODEN: NMBIEO; ISSN: 0883-2897
DT Journal
LA English
CC **8-9** (Radiation Biochemistry)
Section cross-reference(s): 25, 28
GI

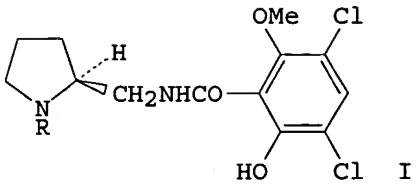


I, R=$(CH_2)_3{}^{18}F$
II, R=H
III, R=$(CH_2)_3F$

AB No-carrier-added (NCA) I [an analog of dopamine D-1 receptor ligand SCH 23390 (II)], Et 8-fluoro-5,6-dihydro-5-(3'-fluoropropyl)-6-oxo-4H-imidazo[1,5-a][1,4]benzodiazepine-3-carboxylate, and 3'-[18F]fluoropropyl 8-fluoro-5,6-dihydro-5-methyl-6-oxo-4H-imidazo[1,5-a][1,4]benzodiazepine-3-carboxylate (analogs of the benzodiazepine RO 15-1788) were synthesized by alkylation of the corresponding nor-compound with NCA 1-[18F]fluoro-3-iodopropane in 10-15% yield (EOB) in .apprx.110 min and with a mass of 2-3 nmol. III is less potent (.apprx.12-14 times) than I in binding to rat striatal membranes in vitro. The other analogs exhibit no specific anatomical distribution to mouse brain. The substituent at position 3 of I, and position 5 and carboxylate group of RO 15-1788 are critical determinants both of affinity and selectivity for receptor binding, and underscores the evaluation necessary when even minor changes (C1 to C3) are made in bioactive compds.
ST fluorine 18 iodopropane dopamine benzodiazepine receptor
IT Heart, metabolism
Kidney, metabolism
Liver, metabolism
Lung, metabolism
Muscle, metabolism

Spleen, metabolism
(benzodiazepine and dopaminergic D1 receptor radioligands distribution in)
IT Brain, metabolism
(preparation and distribution of benzodiazepine and dopaminergic D1 receptor radioligands in)
IT Receptors
RL: SPN (Synthetic preparation); PREP (Preparation)
(benzodiazepine, radioligands for characterization of, benzazepine derivs. as, preparation of)
IT Molecular structure-biological activity relationship
(benzodiazepine receptor-binding, of benzazepine derivs.)
IT Receptors
RL: SPN (Synthetic preparation); PREP (Preparation)
(dopaminergic D1, radioligands for characterization of, benzazepine derivs. as, preparation of)
IT Molecular structure-biological activity relationship
(dopaminergic D1 receptor-binding, of benzazepine derivs.)
IT Intestine, metabolism
(small, benzodiazepine and dopaminergic D1 receptor radioligands distribution in)
IT 352-91-0, 1-Bromo-3-fluoropropane **108607-97-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of benzazepine derivs.)
IT 79089-72-8 84378-44-9 106648-57-1, SCH 24518
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, with labeled and unlabeled halopropanes)
IT 133368-69-1P 133368-70-4P 133368-71-5P 133368-72-6P 133368-73-7P 133368-74-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and affinity and selectivity for benzodiazepine and dopaminergic D1 receptors)
IT **108607-97-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of benzazepine derivs.)
RN 108607-97-2 HCAPLUS
CN Propane, 1-(fluoro-18F)-3-iodo- (9CI) (CA INDEX NAME)

L99 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1990:532755 HCAPLUS
DN 113:132755
ED Entered STN: 13 Oct 1990
TI N-Fluoroalkylated and N-alkylated analogs of the dopaminergic D-2 receptor antagonist raclopride
AU Lannoye, G. S.; Moerlein, Stephen M.; Parkinson, D.; Welch, M. J.
CS Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
SO Journal of Medicinal Chemistry (**1990**), 33(9), 2430-7
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 34-2 (**Amino Acids, Peptides**, and **Proteins**)
Section cross-reference(s): 1, 25, 27
OS CASREACT 113:132755
GI



I

AB Title fluoroalkylated analogs I [R = (CH2)nF (n = 2, 3, 4), (R)- or (S)-CH2CH2CHFMe] and N-alkylated analogs I (R = Pr, Bu) were synthesized and evaluated as potential dopaminergic receptor-based positron tomog. radiopharmaceuticals. Radiosynthetic procedures for producing I [R = (CH2)n18F (n = 2, 3, 4)] were also developed. In vitro binding assays using competitive displacement of [3H]spiperone from primate caudate tissue indicated that the N-alkylated analogs of raclopride had Ki values of 5-40 nM, whereas the corresponding values for analogous N-fluoroalkylated derivs. ranged from 90-160 nM. The relatively low D-2 binding affinity of these fluorinated salicylamides was corroborated by in vivo tissue biodistribution results in rodents. On the basis of structure-binding correlations, the impact of intramol. hydrogen bonding, ligand basicity, and steric bulk on the affinity of the benzamides for D-2 receptor binding are discussed. Strategies are presented for the development of alternative fluorinated salicylamides that are both receptor active and metabolically stable.

ST raclopride fluoroalkylated alkylated analog; dopaminergic D2 receptor antagonist raclopride

IT Neurotransmitter antagonists
(dopaminergic D2, raclopride fluoroalkylated and alkylated analogs)

IT Molecular structure-biological activity relationship
(dopaminergic D2 antagonist, of raclopride fluoroalkylated and alkylated analogs)

IT 74-96-4, Ethyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of prolinamide)

IT 762-49-2, 1-Bromo-2-fluoroethane
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of pyrrolidine derivative)

IT 97849-50-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, with fluoroalkyl-18F iodides)

IT 98598-84-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of, with benzoyl chloride derivative)

IT **762-52-7P 108607-97-2P 128843-36-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation by, of pyrrolidine derivative)

IT 128843-17-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and detritylation of)

IT 98598-85-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and fluoroalkylation of)

IT 82935-40-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydride reduction of)

IT 128843-18-5P 128843-19-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and partial O-demethylation of)
IT 114812-34-9P 114812-35-0P 128843-29-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and sequential hydride reduction, N-benzoylation, and partial-O-demethylation of)
IT 84225-95-6P 98185-20-7P 128843-20-9P 128843-22-1P 128843-24-3P
128843-26-5P 128843-28-7P 128843-31-2P 128843-33-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 124840-52-4P 128843-21-0P 128843-23-2P 128843-25-4P 128843-27-6P
128843-30-1P 128843-32-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as dopaminergic D-2 receptor antagonist)
IT 124840-49-9P 128843-37-8P 128843-38-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as potential dopaminergic receptor-based positron tomog. radiopharmaceutical)
IT 106114-40-3 128843-34-5 128843-35-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with fluoride-18)
IT 76-83-5, Trityl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(tritylation by, of prolinamide)
IT 7531-52-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(tritylation of, with trityl chloride)
IT 32541-62-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-acylation by, of (aminomethyl)pyrrolidine)
IT **762-52-7P 108607-97-2P 128843-36-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation by, of pyrrolidine derivative)
RN 762-52-7 HCAPLUS
CN Ethane, 1-(fluoro-18F)-2-iodo- (7CI, 8CI, 9CI) (CA INDEX NAME)

$^{18}F-CH_2-CH_2-I$

RN 108607-97-2 HCAPLUS
CN Propane, 1-(fluoro-18F)-3-iodo- (9CI) (CA INDEX NAME)

$^{18}F-CH_2-CH_2-CH_2-I$

RN 128843-36-7 HCAPLUS
CN Butane, 1-(fluoro-18F)-4-iodo- (9CI) (CA INDEX NAME)

$^{18}F-(CH_2)_4-I$

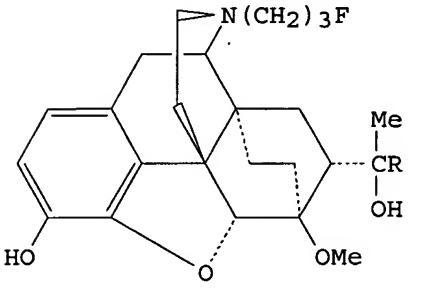
L99 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1990:494069 HCAPLUS
DN 113:94069
ED Entered STN: 16 Sep 1990
TI No-carrier-added (NCA) N-(3-[18F]fluoropropyl)-N-norbuprenorphine and

N-(3-[18F]fluoropropyl)-N-nordiprenorphine - synthesis, anatomical distribution in mice and rats, and tomographic studies in a baboon

AU Bai, Lanqin; Teng, Renrui; Shiue, Chyngyann; Wolf, Alfred P.; Dewey, Stephen L.; Holland, M. Jean; Simon, Eric J.
CS Chem. Dep., Brookhaven Natl. Lab., Upton, NY, 11973, USA

SO Nuclear Medicine and Biology (**1990**), 17(2), 217-27
CODEN: NMBIEO; ISSN: 0883-2897
DT Journal
LA English
CC **8-10** (Radiation Biochemistry)

GI



I, R=CMe3
II, R=Me

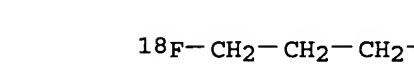
AB N-(3-Fluoropropyl)-N-norbuprenorphine (I) and N-(3-fluoropropyl)-N-nordiprenorphine (II) were synthesized by N-alkylation of norbuprenorphine and nordiprenorphine with 1-bromo-3-fluoropropane. The corresponding no-carrier-added (NCA) N-(3-[18F]fluoropropyl)-N-norbuprenorphine (III) and N-(3-[18F]fluoropropyl)-N-nordiprenorphine (IV) were synthesized by N-alkylation of norbuprenorphine and nordiprenorphine with NCA 1-[18F]fluoro-3-iodopropane in a synthesis time of .apprx.100 min from end of bombardment (EOB) with an overall radiochem. yield of .apprx.15% (EOB) and a mass of 2-3 nmol. In vitro studies indicate that in the absence of NaCl, compds. I, II, N-propyl-N-norbuprenorphine (V), buprenorphine, and diprenorphine are reasonably comparable in binding affinity for opioid receptors. In the presence of 100 nM NaCl, however, compds. I, II, and V, are clearly less potent than buprenorphine and diprenorphine. The anatomical distribution study of compound III in mice shows radioactivity accumulating in bone, indicating that in vivo defluorination may have occurred. Rat studies of both compds. III and IV indicate the specific distribution of these 2 radioligands within certain cortical and subcortical regions of rat brain. However, the absolute uptake of compound IV in rat brain was only half that of compound III. PET studies of III in a baboon revealed specific binding of compound III in striatum and cerebellum. At 1 h after injection, ratios of specific/nonspecific binding of III in striatum and cerebellum of a baboon were 1.9 and 1.7, resp.

ST fluorine 18 fluoropropylnorbuprenorphine fluoropropylnordiprenorphine prepn tomog; tomog brain fluorine 18 fluoropropylnorbuprenorphine fluoropropylnordiprenorphine; positron emission tomog brain radioligand

IT Bone, metabolism
Heart, metabolism
Kidney, metabolism
Liver, metabolism
Lung, metabolism
Muscle, metabolism
Spleen, metabolism
(fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)

IT Blood
Organ
(fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine distribution in, positron emission tomog. of brain in relation to)
IT Brain
(positron emission tomog. of, fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine preparation for)
IT Brain, metabolism
(amygdaloid body, fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT Brain, metabolism
(cerebellum, fluorine-18-fluoropropylnorbuprenorphine and -fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT Spinal cord
(cervical, fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT Spinal column
(cervical vertebra, fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT Brain, metabolism
(hippocampus, fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT Receptors
RL: BIOL (Biological study)
(opioid, buprenorphine and diprenorphine and fluoroalkyl derivs. affinity for, positron emission tomog. of brain in relation to)
IT Tomography
(positron-emission, of brain, fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine preparation for)
IT Brain, metabolism
(prosencephalon, basal, fluorine-18-fluoropropylnorbuprenorphine and -fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT Intestine, metabolism
(small, fluorine-18-labeled fluoropropylnorbuprenorphine and fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT Brain, metabolism
(stem, fluorine-18-fluoropropylnorbuprenorphine and -fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT Brain, metabolism
(striatum, fluorine-18-fluoropropylnorbuprenorphine and -fluoropropylnordiprenorphine biodistribution and metabolism in, positron emission tomog. of brain in relation to)
IT 78715-23-8, Norbuprenorphine 101330-58-9, Nordiprenorphine
RL: BIOL (Biological study)
(alkylation of and opioid receptors of brain affinity for)
IT 125828-28-6P 128837-82-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and biodistribution of and opioid receptors of brain affinity for, positron emission tomog. in relation to)
IT 89663-71-8P, N-Propyl-N-norbuprenorphine 125828-20-8P, N-(3-Fluoropropyl)-N-nordiprenorphine 128837-83-2P, N-(3-Fluoropropyl)-N-norbuprenorphine

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and opioid receptors of brain affinity for)
IT 107-08-4, 1-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with norbuprenorphine)
IT 352-91-0, 1-Bromo-3-fluoropropane **108607-97-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with norbuprenorphine or nordiprenorphine)
IT **108607-97-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with norbuprenorphine or nordiprenorphine)
RN 108607-97-2 HCAPLUS
CN Propane, 1-(fluoro-18F)-3-iodo- (9CI) (CA INDEX NAME)



L99 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1990:459639 HCAPLUS
DN 113:59639
ED Entered STN: 17 Aug 1990
TI Comparison of bromo- and iodoalkyl triflates for fluorine-18-radiolabeling of amines
AU Chesis, Paul L.; Welch, Michael J.
CS Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
SO Applied Radiation and Isotopes (**1990**), 41(3), 259-65
CODEN: ARISEF; ISSN: 0883-2889
DT Journal
LA English
CC 31-3 (Alkaloids)
Section cross-reference(s): **8**
AB The use of 3-bromopropyl trifluoromethanesulfonate and 3-iodopropyl trifluoromethanesulfonate (triflates) as precursors for 18F-labeling of a secondary amine is described. This simple two step procedure, [18F]fluoride triflate displacement followed by N-alkylation, has been optimized using N-nordiprenorphine as the model substrate. The highest radiochem. yields (85%) for the triflate displacement reaction were obtained in THF using Bu4NOH as the base. In comparing the two triflates no differences in the yields for this step were observed In contrast, the yields for the fluoroalkylation step were increased more than 75% by using 1-[18F]fluoro-3-iodopropane rather than 1-bromo-3-[18F]fluoropropane. The highest yields for this N-alkylation reaction (35%) were achieved in DMF using N,N-diisopropylethylamine as the base. For both steps the observed yields are strongly dependent on the relative concns. of the major reactants.
ST bromoalkyl triflate amine fluorine radiolabeling; iodoalkyl triflate amine fluorine radiolabeling
IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(secondary, fluorine-18 radiolabeling of, bromoalkyl and iodoalkyl triflate for)
IT 93617-83-5 107371-67-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(displacement reaction of, with iodoalkyl triflate)
IT 352-91-0P, 1-Bromo-3-fluoropropane 462-40-8P, 1-Fluoro-3-iodopropane
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation by, of N-nordiprenorphine)
IT **108607-97-2P 108607-98-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and N-alkylation by, of N-nordiprenorphine)
IT 125828-20-8P 125828-28-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 103935-48-4P, 3-Bromopropyl trifluoromethanesulfonate 106114-40-3P, 3-Iodopropyl trifluoromethanesulfonate
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as precursor for fluorine-18 radiolabeling of secondary amines)
IT 38078-09-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with alkylpropanol)
IT 358-23-6, Trifluoromethanesulfonic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with iodopropanol)
IT 627-18-9, 3-Bromo-1-propanol 627-32-7, 3-Iodo-1-propanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with trifluoromethanesulfonic anhydride)
IT 101330-58-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation of)
IT **108607-97-2P 108607-98-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and N-alkylation by, of N-nordiprenorphine)
RN 108607-97-2 HCAPLUS
CN Propane, 1-(fluoro-18F)-3-iodo- (9CI) (CA INDEX NAME)

$^{18}F-CH_2-CH_2-CH_2-I$

RN 108607-98-3 HCAPLUS
CN Propane, 1-bromo-3-(fluoro-18F)- (9CI) (CA INDEX NAME)

$Br-CH_2-CH_2-CH_2-^{18}F$

L99 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1990:194599 HCAPLUS
DN 112:194599
ED Entered STN: 26 May 1990
TI Preparation and use of no-carrier-added (18F)-N-fluoroalkylspiroperidols
IN Shiue, Chyng Yann; Wolf, Alfred P.; Bai, Lan Qin; Teng, Ren Tui
PA United States Dept. of Energy, USA
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K049-02
ICS C07D471-10
NCL 424001100
CC **8-9** (Radiation Biochemistry)
Section cross-reference(s): 28
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4871527	A	19891003	US 1987-43824	19870429 <--
PRAI US 1987-43824		19870429 <--		

CLASS
PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

US 4871527	ICM	A61K049-02
	ICS	C07D471-10
	NCL	424001100

AB The title compds. (the alkyl contains 2-6 C) are prepared and used in positron-emission transaxial tomog., especially for mapping dopamine receptors in normal and diseased mammalian brains. Spiroperidol and tetrabutylammonium hydroxide were reacted with no-carrier-added 1-[18F]fluoro-3-iodopropane (prepared from K[18F] and (CH2)3I2) in pentane to give N-(o-[18F]fluoropropyl)spiroperidol (I) in a 20% yield. Metabolic and kinetic studies were made for I in blood and brain.

ST fluorine 18 labeled spiroperidol prepn; positron emission transaxial tomog spiroperidol deriv; dopamine receptor brain tomog spiroperidol deriv

IT Brain, composition
(dopamine receptors of, mapping of, by positron-emission transaxial tomog., fluorine-18-labeled spiroperidol for)

IT Brain, metabolism
(cerebellum, fluorine-18-labeled spiroperidol metabolism by)

IT Receptors
RL: BIOL (Biological study)
(dopaminergic, mapping of, of brain, by positron-emission transaxial tomog., fluorine-18-labeled spiroperidol for)

IT Tomography
(positron-emission, transaxial, dopamine receptors of brain mapping by, fluorine-18-labeled spiroperidols for)

IT Brain, metabolism
(striatum, fluorine-18-labeled spiroperidol metabolism by)

IT 749-02-0, Spiroperidol
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, with no-carrier-added fluorine-18 fluoralkyl halide)

IT 749-02-0D, Spiroperidol, fluorine-18-N-fluoroalkyul derivs.
RL: BIOL (Biological study)
(no-carrier-added, for positron-emission transaxial tomog.)

IT 107480-31-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and biol. properties of no-carrier-added)

IT **762-52-7P** 85725-77-5P **108607-97-2P**
108607-98-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 107340-59-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of no-carrier-added)

IT 53612-91-2, Potassium fluoride (K18F)
RL: BIOL (Biological study)
(reaction of no-carrier-added, with alkyl halides)

IT 106-93-4 109-64-8 624-73-7 627-31-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with no-carrier-added fluorine-18 potassium fluoride)

IT **762-52-7P 108607-97-2P 108607-98-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 762-52-7 HCAPLUS

CN Ethane, 1-(fluoro-18F)-2-iodo- (7CI, 8CI, 9CI) (CA INDEX NAME)

$^{18}F-CH_2-CH_2-I$

RN 108607-97-2 HCAPLUS

CN Propane, 1-(fluoro-18F)-3-iodo- (9CI) (CA INDEX NAME)

$^{18}F-CH_2-CH_2-CH_2-I$

RN 108607-98-3 HCAPLUS
CN Propane, 1-bromo-3-(fluoro-18F)- (9CI) (CA INDEX NAME)

$Br-CH_2-CH_2-CH_2-^{18}F$

L99 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:204176 HCAPLUS
DN 108:204176
ED Entered STN: 11 Jun 1988
TI Applied carrier-free 18F-fluoroalkylation and 18F-fluoroacylation
AU Block, Dirk
CS Univ. Koeln, Cologne, D 38, Fed. Rep. Ger.
SO Ber. Kernforschungsanlage Juelich (**1987**), Juel-2122, 131 pp.
CODEN: BKEJAS; ISSN: 0366-0885
DT Report
LA German
CC 23-1 (Aliphatic Compounds)
Section cross-reference(s): **8**, 25, 28
AB Preparation and introduction of no-carrier-added (n.c.a.) [18F]-fluoroalkyl and n.c.a. [18F]-fluoracyl moieties as small groups were studied as alternatives to n.c.a. labeling via direct nucleophilic substitution. Starting materials for the n.c.a. [18F]-fluoroalkylation, and n.c.a. [18F]fluoroacylation were sym. disubstituted alkanes and α-substituted carboxylic acid esters, resp. The nucleophilic fluorination of these precursors were systematically investigated with regard to the effect of various important reaction parameters. The monofluorinated groups, both monfluorinated alkanes and α-fluorinated carboxylic acid esters, were obtained under optimized conditions with radiochem. yields of about 90% using the efficient fluorination system, aminopolyether 2.2.2/K2CO3 in MeCN as solvent. The n.c.a. [18F]-fluoroalkylation of protic functional groups via condensation was performed as a one pot synthesis under basic conditions. The radiochem. yields of these condensation reactions depended on the acid constant of the organic substrates. The highest yields of about 90% of fluoroalkylated products were achieved in MeCN with phenols as substrates and n.c.a. [18F]-fluorotosyloxyalkanes as the most valuable fluoroalkylating agents. The n.c.a. [18F]-fluoroacylation of -OH and -NHR functional groups were carried out in 2 steps. The highest yields of about 85% of fluoroacylated products were obtained in the presence of acids in polar protic solvents when simple primary amines were used as substrates and α-fluoropropionic acid methyl ester as the best n.c.a. [18F]-fluoroacylating agent. The [18F]-fluoroalkylation via bistosyloxyalkanes was applied to the synthesis of n.c.a. [18F]-fluoroalkylspiperones, potent dopamine receptor ligands to be used for receptor mapping in conjunction with positron emission tomog.
ST fluorine 18 fluoroalkylation fluoroacylation
IT Solvent effect
(on fluorine-18 fluoroalkylation and fluoroacylation)
IT Acylation
(fluoro-, with fluorine-18-labeled compds.)
IT Haloalkylation
(fluoroalkylation, with fluorine-18-labeled compds.)
IT 74-95-3 106-93-4 109-64-8, 1,3-Dibromopropane 156-72-9 4672-49-5 5469-66-9 6315-52-2 15886-84-7 24124-59-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(fluoride-18 substitution reaction of)
IT 64-17-5, uses and miscellaneous 67-64-1, uses and miscellaneous

75-05-8, uses and miscellaneous 75-09-2, uses and miscellaneous
109-99-9, uses and miscellaneous 123-91-1, uses and miscellaneous
RL: USES (Uses)
(fluorine-18 fluoroalkylation and fluoroacylation in)

IT 749-02-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(fluoroalkylation of, with fluorine-18-labeled fluoroalkyl derivs.)

IT 53334-02-4P 60520-16-3P 85725-77-5P 104839-79-4P 107340-59-0P
108607-98-3P 109483-48-9P 113426-11-2P **113426-12-3P**
113426-13-4P 113426-14-5P 113426-15-6P 113426-16-7P 114435-78-8P
114435-79-9P 114435-80-2P 114435-81-3P 114435-82-4P 114435-83-5P
114435-84-6P 114435-85-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 312-68-5P 349-43-9P, Ethyl 2-fluoropropionate 352-91-0P,
Fluorobromopropane 372-04-3P, Fluoromesyloxypropane 383-50-6P,
Fluorotosyloxyethane 404-15-9P, Fluoroacetic acid phenyl ester
404-45-5P, Fluoroacetic acid p-chlorophenyl ester 405-56-1P,
Fluoroacetic acid p-nitrophenyl ester 405-72-1P, β-Fluoroethyl
p-chlorophenyl ether 405-97-0P, β-Fluoroethyl phenyl ether
442-31-9P 453-18-9P, Methyl fluoroacetate 459-72-3P, Ethyl
fluoroacetate 461-31-4P, Fluoromesyloxyethane 462-24-8P,
1-Fluoro-3-nitropropane 762-49-2P, Fluorobromoethane 2366-56-5P
63186-89-0P, N-β-Fluoroethyl benzamide 70659-93-7P,
γ-Fluoropropyl phenyl ether 101803-69-4P, β-Fluoroethyl
benzyl ether 106114-42-5P 114435-86-8P, Fluorotosyloxymethane
114435-87-9P, Fluoromesyloxymethane 114435-88-0P, α-Fluoro-p-
chloroanisole 114435-89-1P 114435-90-4P, Fluoroacetic acid p-anisyl
ester 114435-91-5P 114435-92-6P, Propyl 2-fluoropropionate 114435-93
-7P, Isopropyl 2-fluoropropionate 114435-94-8P, Butyl 2-fluoropropionate
114435-95-9P, Isobutyl 2-fluoropropionate 114449-13-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, fluorine-18 fluoroalkylation and fluoroacylation in
relation to)

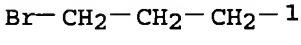
IT 39794-75-7P, Ethyl tosyloxyacetic acid
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, in fluoroalkyl derivs. preparation)

IT 96-32-2, Methyl α-bromoacetate 105-36-2, Ethyl
α-bromoacetate 620-72-4, Phenyl α-bromoacetate 3395-91-3
5445-17-0 19199-82-7, p-Nitrophenyl bromoacetate 38829-10-6
38829-11-7 60477-29-4, p-Methoxyphenyl bromoacetate
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with fluoride-18)

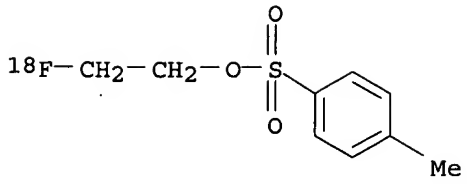
IT 106-48-9, p-Chlorophenol 108-95-2, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with fluorine-18-labeled fluoroalkyl
derivs.)

IT **108607-98-3P 113426-12-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

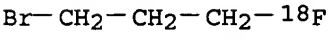
RN 108607-98-3 HCAPLUS
CN Propane, 1-bromo-3-(fluoro-18F)- (9CI) (CA INDEX NAME)



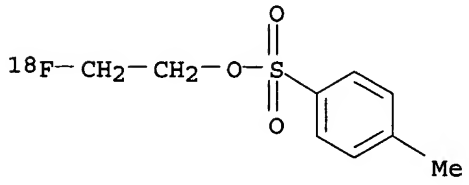
RN 113426-12-3 HCAPLUS
CN Ethanol, 2-(fluoro-18F)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)



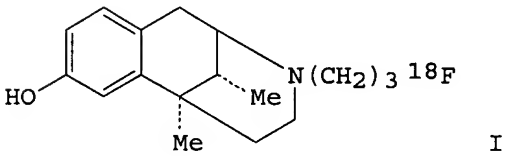
L99 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:130967 HCAPLUS
DN 108:130967
ED Entered STN: 15 Apr 1988
TI The N.C.A. nucleophilic 18F-fluorination of 1,N-disubstituted alkanes as fluoroalkylation agents
AU Block, Dirk; Coenen, Heinz Hubert; Stoecklin, Gerhard
CS Inst. Chemie 1 (Nuklearchem.), Kernforschungsanlage Juelich G.m.b.H., Juelich, D-5170, Fed. Rep. Ger.
SO Journal of Labelled Compounds and Radiopharmaceuticals (**1987**), 24(9), 1029-42
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA English
CC 23-3 (Aliphatic Compounds)
OS CASREACT 108:130967
AB R(CH2)n18F (R = Br, MeSO3, 4-MeC6H4SO3; n = 1-3) were prepared in radiochem. yields up to 89% by treating R(CH2)nR with 18F- supported on an aminopolyether-K2CO3 complex. Thus, MeSO3(CH2)2O3SMe was treated with Kryptofix 2.2.2-K2CO3-18F- in MeCN to give MeSO3(CH2)218F in a radiochem. yield of 77%. The substitution yield increased with increasing chain length and with the leaving group sequence Br- > MeSO3- > 4-MeC6H4SO3-.
ST nucleophilic fluorine 18 fluorination disubstituted alkane; substituted alkane fluorination; aminopoly ether supported fluoride; potassium carbonate aminopoly ether complex; bromo fluoroalkane; fluoroalkyl mesylate; labeled alkyl fluoride prepn
IT **Fluorination**
(of disubstituted alkanes with labeled fluoride)
IT 7782-41-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(fluorination, of disubstituted alkanes with labeled fluoride)
IT 24124-59-2P 85725-77-5P 104839-79-4P **108607-98-3P**
113426-11-2P **113426-12-3P** 113426-13-4P 113426-14-5P
113426-15-6P 113426-16-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 74-95-3 106-93-4 109-64-8, 1,3-Dibromopropane 156-72-9 4672-49-5, 1,2-Bis(mesyloxy)ethane 5469-66-9 6315-52-2 15886-84-7, 1,3-Bis(mesyloxy)propane
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with labeled fluoride in presence of aminopolyether-potassium carbonate)
IT **108607-98-3P 113426-12-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 108607-98-3 HCAPLUS
CN Propane, 1-bromo-3-(fluoro-18F)- (9CI) (CA INDEX NAME)



RN 113426-12-3 HCAPLUS
CN Ethanol, 2-(fluoro-18F)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)



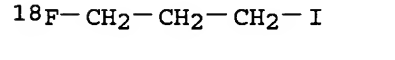
L99 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1987:473461 HCAPLUS
DN 107:73461
ED Entered STN: 05 Sep 1987
TI No-carrier-added (NCA) (±)-N-(3-[18F]fluoropropyl)-N-normetazocine - synthesis and PET studies in a baboon
AU Shiue, Chyng Yann; Teng, Renrui; Bai, Lanqin; Wolf, Alfred P.; Arnett, Carroll D.; Simon, Eric J.
CS Chem. Dep., Brookhaven Natl. Lab., Upton, NY, 11973, USA
SO Nuclear Medicine and Biology (**1987**), 14(2), 119-22
CODEN: NMBIEO; ISSN: 0883-2897
DT Journal
LA English
CC **8-9** (Radiation Biochemistry)
Section cross-reference(s): 63
GI



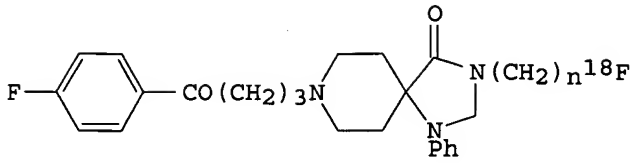
I

AB NCA (±)-N-(3-[18F]fluoropropyl)-N-normetazocine (I) was synthesized by N-alkylation of (±)-N-normetazocine with NCA 1-[18F]fluoro-3-iodopropane in an overall radiochem. yield of 10% with a mass of 3.5 nmol in a synthesis time of 90 min from end of bombardment. Positron emission tomog. (PET) studies of I in a baboon did not indicate specificity for opiate receptor sites alone. The activity declined rapidly in the striatum, the frontal cortex, and the cerebellum. The baboon total arterial plasma radioactivity clearance was very rapid and the metabolism of I in plasma was also very rapid. These results suggest that I is not a suitable radioligand for imaging opiate receptors in the human brain by PET.
ST fluorine 18 fluoropropylnormetazecine prepn; positron emission tomog opiate receptor; brain positron tomog fluorine 18
IT Blood plasma
(fluorine-18-labeled flouropropylnormetazocine distribution and clearance from, brain opiate receptors positron emission tomog. in relation to)
IT Receptors
RL: PROC (Process)
(for opiates, in brain, positron emission tomog. of, with

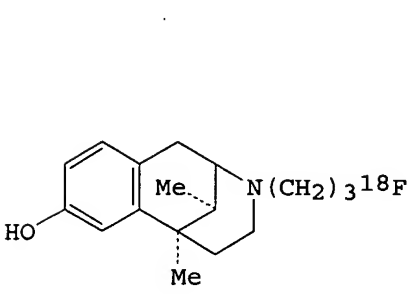
fluorine-18-labeled fluoropropylnormetazocine)
IT Brain, composition
(opiate receptors of, positron emission tomog. of, with fluorine-18-labeled fluoropropylnormetazocine)
IT Opiates and Opioids
RL: BIOL (Biological study)
(receptors for, of brain, positron emission tomog. of, with fluorine-18-labeled fluoropropylnormetazocine)
IT Tomography
(positron-emission, of brain opiate receptors, with fluorine-18-labeled fluoropropylnormetazocine)
IT 108607-95-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and positron emission tomog. with, of brain opiate receptors)
IT **108607-97-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and N alkylation with, of normetazocine)
IT 53612-91-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with diiodopropane)
IT 627-31-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with potassium fluoride-18)
IT 25144-78-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation of, with fluorine-18-labeled fluoroiodopropane)
IT **108607-97-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and N alkylation with, of normetazocine)
RN 108607-97-2 HCAPLUS
CN Propane, 1-(fluoro-18F)-3-iodo- (9CI) (CA INDEX NAME)



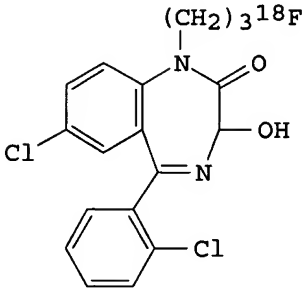
L99 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1987:439756 HCAPLUS
DN 107:39756
ED Entered STN: 08 Aug 1987
TI Synthesis of no-carrier-added (NCA) [18F]fluoroalkyl halides and their application in the syntheses of [18F]fluoroalkyl derivatives of neurotransmitter receptor active compounds
AU Shiue, C. Y.; Bai, L. Q.; Teng, R. R.; Wolf, A. P.
CS Chem. Dep., Brookhaven Natl. Lab., Upton, NY, 11973, USA
SO Journal of Labelled Compounds and Radiopharmaceuticals (**1987**), 24(1), 55-64
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA English
CC 28-18 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **8**, 23, 27, 63
GI



I, n=2
II, n=3



III



IV

AB Spiroperidol derivs., I and II, (±)-N-(3-[18F]fluoropropyl)normetazocin e (III) and N-(3-[18F]fluoroproyl)lorazepam (IV) were prepared by alkylation with 18F(CH2)nX (X = halide and n = 2 or 3) which were prepared by nucleophilic aliphatic substitution of alkyl halides with NCA 18F- in MeCN. These radioligands can be used in positron emission tomog. or receptor-binding studies.

ST fluoro 18 neurotransmitter; spiroperidol fluoro 18 alkyl; metrazocine fluoro 18 alkyl; lorazepam fluoro 18 alkyl

IT 749-02-0, Spiroperidol 846-49-1, Lorazepam 16808-63-2, Normetazocine
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, with fluoride-18)

IT **762-52-7P** 85725-77-5P **108607-97-2P** **108607-98-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with drug substrates)

IT 53612-91-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and substitution reaction with dihaloalkanes)

IT 106114-42-5P 106114-44-7P 107340-59-0P 107480-31-9P 108607-95-0P 108607-96-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

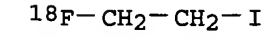
IT 352-91-0, 1-Bromo-3-fluoropropane 762-49-2, 1-Bromo-2-fluoroethane
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with spiroperidol)

IT 106-93-4, 1,2-Dibromoethane 109-64-8, 1,3-Dibromopropane 624-73-7, 1,2-Diiodoethane 627-31-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with fluoride-18)

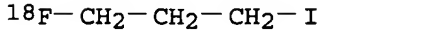
IT **762-52-7P 108607-97-2P 108607-98-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with drug substrates)

RN 762-52-7 HCAPLUS

CN Ethane, 1-(fluoro-18F)-2-iodo- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 108607-97-2 HCAPLUS
CN Propane, 1-(fluoro-18F)-3-iodo- (9CI) (CA INDEX NAME)



RN 108607-98-3 HCAPLUS
CN Propane, 1-bromo-3-(fluoro-18F)- (9CI) (CA INDEX NAME)

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